VOL. XXXIV. SEPTEMBER, 1905. NO. 3.

# AMERICAN

# CHEMICAL JOURNAL

Contributions from the Sheffield Laboratory of Yale University.

## CXXV.—RESEARCHES ON PYRIMIDINES: THE ACTION OF AQUEOUS AND ALCOHOLIC AMMONIA AND ANILINE ON SOME HALOGEN AND MERCAPTO PYRIMIDINES.

[TENTH PAPER.]

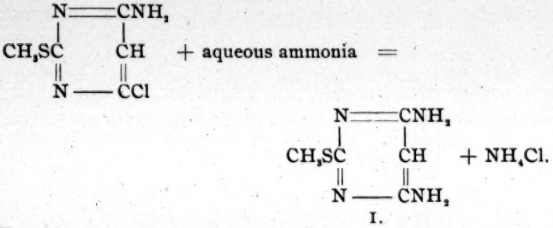
BY TREAT B. JOHNSON AND CARL O. JOHNS.

The object of this paper is to describe the behavior of certain halogen and mercapto pyrimidines towards ammoniacal solutions and aniline.

We have had occasion, in the preparation of aminopyrimidines, to use both aqueous and alcoholic solutions of ammonia to replace, with the amino group, halogens and mercapto radicals in pyrimidines. We have been greatly impressed, in the course of this work, with the remarkable difference in degree of reactivity of aqueous and alcoholic ammonia towards such pyrimidine derivatives.

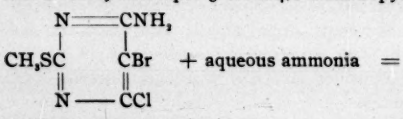
In a recent publication from this laboratory, by Wheeler and

Jamieson,[1] it was shown that when 2-methylmercapto-5-methyl-4,6-dichlorpyrimidine was heated with alcoholic methylamine, only 1 chlorine atom was removed and 2-methylmercapto-4-chlor-5-methyl-6-methylamino pyrimidine was the product of the reaction. An analogous result was obtained when 2-methylmercapto-4,6-dichlorpyrimidine was heated with alcoholic ammonia. It was converted, practically quantitatively, into 2-methylmercapto-4-chlor-6-aminopyrimidine. They did not succeed in converting this chloraminopyrimidine into the corresponding diaminopyrimidine (I.) by heating with alcoholic ammonia. We now find that the 2-methylmercapto-4-chlor-6-aminopyrimidine is converted, quantitatively, into 2-methylmercapto-4,6-diaminopyrimidine (I.) when heated with aqueous ammonia, at 185°–195°:

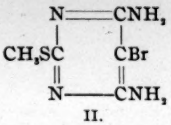


I.

It seemed of interest, in connection with this result, to compare the behavior of aqueous and alcoholic ammonia towards 2-methylmercapto-4-chlor-5-brom-6-aminopyrimidine. This compound reacts in an analogous manner to the above 2-methylmercapto-4-chlor-6-aminopyrimidine. It can be recovered unaltered after heating with concentrated alcoholic ammonia, at 150°–160°. When heated with aqueous ammonia, under the same conditions, (150°–160°), it was converted, quantitatively, into 2-methylmercapto-5-brom-4,6-diaminopyrimidine,

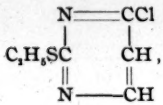


[1] THIS JOURNAL, 32, 343 (1904).

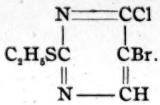


II.

It would appear, from the results of these two experiments, that a halogen is more easily replaced by the amino group when aqueous ammonia is used. In order to test this assumption further and to compare the action of ammoniacal solutions in another series, we have examined the comparative behavior of 2-ethylmercapto-6-chlorpyrimidine (III.) and 2-ethylmercapto-5-brom-6-chlorpyrimidine[1] (IV.) towards aqueous and alcoholic ammonia:



III.



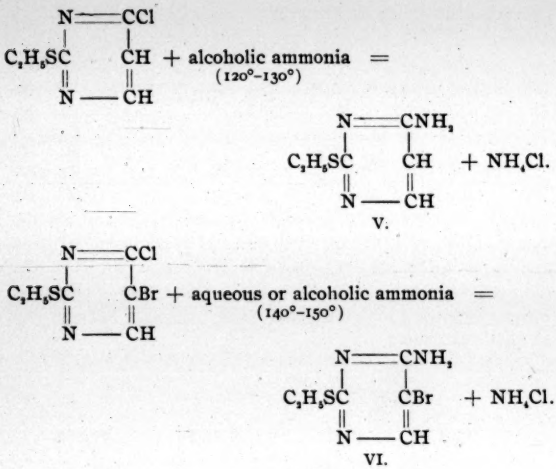
IV.

Wheeler and Johnson[2] observed that 2-ethylmercapto-6-chlorpyrimidine reacts with alcoholic ammonia, at 140°–150°, to form 2-ethylmercapto-6-aminopyrimidine[3] (V.). We now find that this same chlorpyrimidine can be heated with aqueous ammonia, at the same temperature, (140°–150°) and be recovered unaltered. A most remarkable case of lack of analogy was observed when we examined the behavior of ammoniacal solutions towards 2-ethylmercapto-5-brom-6-chlorpyrimidine (IV.). This pyrimidine was converted, quantitatively, into 2-ethylmercapto-5-brom-6-aminopyrimidine (VI.) when heated with alcoholic ammonia, at 120°–130° and also when heated with aqueous ammonia, at 140°–150°.

[1] Wheeler and Johnson: THIS JOURNAL, 31, 603 (1904).

[2] *Ibid.*, 29, 492 (1903).

[3] It has been our experience, since the publication of this paper, that the best yield of this 2-ethylmercapto-6-aminopyrimidine is obtained when the chloride is heated with alcoholic ammonia, at 120°–130°, for 3 or 4 hours. T. B. J.

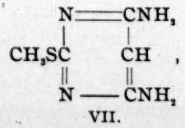



V.

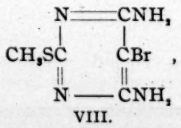



VI.

The abnormal behavior of ammoniacal solutions was also illustrated when we tried to replace the mercapto radical, in certain pyrimidines, with the amino group. 2-Methylmercapto-4,6-diaminopyrimidine[1] (VII.) and 2-methylmercapto-5-brom-4,6-diaminopyrimidine (VIII.) were recovered unaltered, after heating with both aqueous and alcoholic ammonia, at 205°–215°. These two negative results were of especial interest




VII.

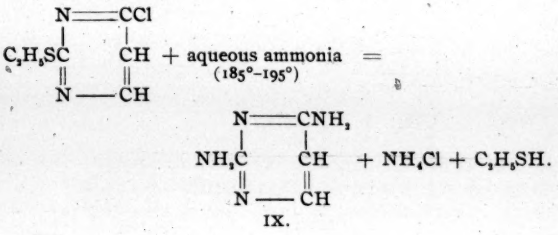



VIII.

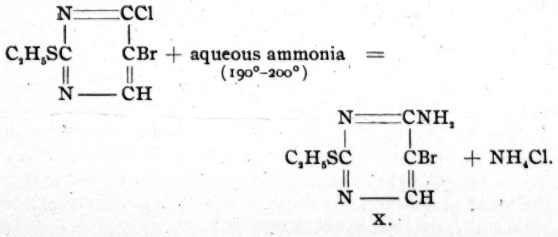
when compared with the behavior of 2-ethylmercapto-6-chlorpyrimidine[2] and 2-ethylmercapto-5-brom-6-chlorpyrimidine[3] towards aqueous ammonia, at high temperatures. When

[1] Wheeler and Jamieson: *Loc. cit.*
[2] Wheeler and Johnson: THIS JOURNAL, 29, 496 (1903).
[3] Wheeler and Johnson: *Ibid.*, 31, 603 (1904).

2-ethylmercapto-6-chlorpyrimidine was heated with aqueous ammonia, at 185°–195°, 2,6-diaminopyrimidine[1] (IX) was the product of the reaction. On the other hand, when 2-ethylmercapto-5-brom-6-chlorpyrimidine was heated, under practically the same conditions, (190°–200°) with aqueous ammonia, the chlorine atom only was removed and 2-ethylmercapto-5-brom-6-aminopyrimidine (X.) was formed:



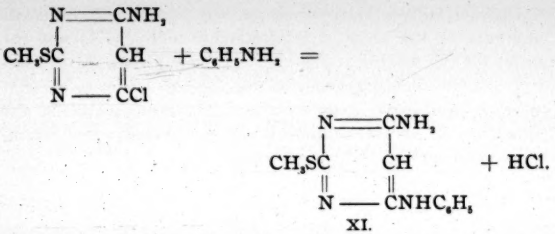

IX.

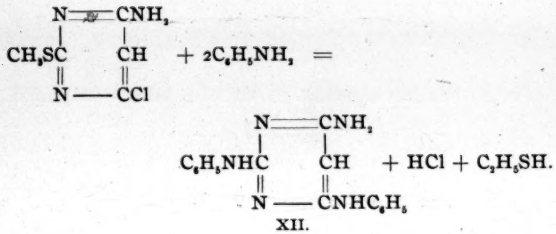



X.

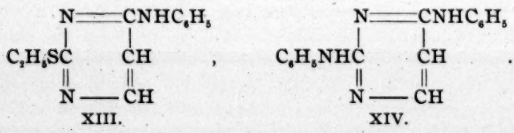
It has been our experience that a mercapto group is more easily replaced by the anilido—$NHC_6H_5$—than by the amino group. When 2-methylmercapto-4-chlor-6-aminopyrimidine was heated with 1 molecular proportion of aniline, at 120°–130°, 2-methylmercapto-4-anilido-6-aminopyrimidine (XI.) was formed. On the other hand, when heated with 2 molecular proportions of aniline, at 140°–150°, 2,4-dianilido-6-aminopyrimidine (XII.) was the product of the reaction.

[1] Büttner: Ber. d. chem. Ges., **36**, 2233.





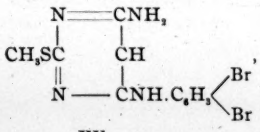
These results are analogous to that obtained by Wheeler and Bristol.[1] They observed that 2-ethylmercapto-6-chlorpyrimidine reacted with 1 molecular proportion of aniline, at 100°, to form 2-ethylmercapto-6-anilidopyrimidine (XIII.). When the same mercaptochlorpyrimidine was heated with 2 molecular proportions of aniline, at 150°, it was converted into 2,6-dianilidopyrimidine (XIV.):



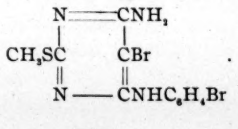
2-Methylmercapto-4-anilido-6-aminopyrimidine (XI.) reacts with bromine, in glacial acetic acid, to form a dibrom substitu-

[1] This Journal, 33, 448 (1905).

tion-product, melting at 202°. In order to establish the structure of this body it was necessary to decide whether 1 or 2 bromine atoms had entered the benzene nucleus; whether 2-methylmercapto-4-dibromanilido-6-aminopyrimidine (XV.) or 2-methylmercapto-4-parabromanilido-5-brom-6-aminopyrimidine (XVI.) was the product of the reaction. The following experiment proved that formula XVI. represents the structure

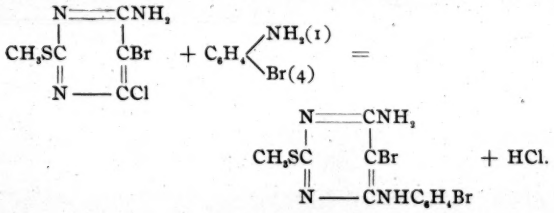


XV.



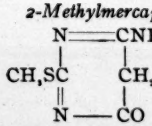
XVI.

of this dibrompyrimidine. The same derivative, melting at 202°, was obtained when 2-methylmercapto-4-chlor-5-brom-6-aminopyrimidine was heated with parabromaniline:



EXPERIMENTAL.

*2-Methylmercapto-4-oxy-6-aminopyrimidine,*



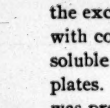
.—This mercaptopyrimidine was easily prepared by dissolving 2-thio-4-oxy-6-aminopyrimidine[1] in alco-

[1] The 2-thio-4-oxy-6-aminopyrimidine used for this preparation was made according to Traube's directions, by condensing thiourea with cyanethylacetate, in presence of sodium ethylate. Ann. Chem. (Liebig), 331, 71.

hol, containing 1 molecular proportion of sodium ethylate and then warming on the steam-bath with 1 molecular proportion of methyl iodide. The reaction is exceedingly smooth and in a few minutes the mercapto derivative separates from the alcoholic solution. The pyrimidine was purified by evaporating the excess of alcohol and then washing the crystalline residue with cold water, to remove sodium iodide. It was difficultly soluble in hot alcohol, from which it separated in colorless plates. It decomposed at 267° with effervescence. The yield was practically quantitative. Analysis :

| | Calculated for $C_5H_7ON_3S$. | Found. |
|---|---|---|
| N | 26.75 | 26.97 |

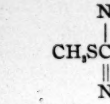
*2-Methylmercapto-4-methoxy-6-aminopyrimidine,*



. — This compound was obtained when 2-thio-4-oxy-6-aminopyrimidine was warmed, in alcohol, with 2 molecular proportions of sodium ethylate and methyl iodide. It was soluble in acids but insoluble in alkali. It was purified by crystallizing from alcohol, from which it separated, on cooling, in long, well-developed prisms. It melted at 256°, without effervescence, to a clear oil. Analysis (Kjeldahl) :

| | Calculated for $C_6H_9ON_3S$. | Found. |
|---|---|---|
| N | 24.55 | 24.46 |

*2-Methylmercapto-4-oxy-5-brom-6-aminopyrimidine,*

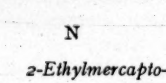


, was prepared by dissolving 2-methylmercapto-4-oxy-6-aminopyrimidine in glacial acetic acid and then adding the calculated quantity of bromine. The bromine color disappeared at once and the pyrimidine separated as a beautiful, crystalline powder. It was difficultly soluble in water and

alcohol. It crystallized from hot acetic acid in slender prisms. It had no definite melting-point, but began to turn brown at 200° and did not melt below 300°. Analysis (Kjeldahl) :

| | Calculated for $C_6H_4ON_3SBr$. | Found. |
|---|---|---|
| N | 17.79 | 17.76 |

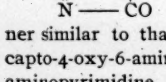
*2-Ethylmercapto-4-oxy-6-aminopyrimidine,*



.—This compound was prepared in a manner similar to that used for the preparation of 2-methylmercapto-4-oxy-6-aminopyrimidine, by warming 2-thio-4-oxy-6-aminopyrimidine, in alcohol, with molecular proportions of sodium ethylate and ethyl bromide. It was very soluble in alcohol. It crystallized from water in long, slender prisms and melted at 216°–217°, to a clear oil. Analysis (Kjeldahl) :

| | Calculated for $C_6H_9ON_3S$. | Found. |
|---|---|---|
| N | 24.56 | 24.37 |

*2-Methylmercapto-4-chlor-6-aminopyrimidine,*



.—This derivative was previously described by Wheeler and Jamieson,[1] who obtained it by heating 2-methylmercapto-4,6-dichlorpyrimidine with alcoholic ammonia. We find that it can be prepared more easily by treating 2-methylmercapto-4-oxy-6-aminopyrimidine with phosphorus oxychloride. The pyrimidine was boiled with an excess of phosphorus oxychloride until the evolution of hydrochloric acid ceased. The clear solution which resulted was then heated to 100°, under diminished pressure, to remove the excess of phosphorus oxychloride. A brittle, amorphous residue was obtained. This proved to be a mixture of the hydrochloride of the unaltered pyrimidine and an unstable phosphorus de-

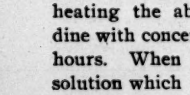
[1] THIS JOURNAL, 32, 343 (1904).

rivative of the mercaptochlorpyrimidine. The amorphous residue was carefully decomposed with ice-water. We obtained a clear, yellow solution, which was then made distinctly alkaline with ammonium hydroxide and concentrated by evaporation on the steam-bath. Upon cooling, a crystalline product separated which proved to be a mixture of the 2-methylmercapto-4-chlor-6-aminopyrimidine and unaltered 2-methylmercapto-4-oxy-6-aminopyrimidine. A separation of the two compounds was effected by washing with dilute sodium hydroxide solution, in which the chlorpyrimidine is insoluble. It was further purified by recrystallizing from water. It agreed in all its properties with the compound described by Wheeler and Jamieson,[1] except that we found it to melt at 132° instead of 126°–127°. Analysis (Kjeldahl):

| | Calculated for $C_5H_6N_3SCl$. | Found. |
|---|---|---|
| N | 23.93 | 23.86 |

In our experiments in the preparation of the above 2-methylmercapto-4-chlor-6-aminopyrimidine we have usually obtained only about 45–50 per cent of the theoretical yield. In one experiment the yield corresponded to 59.6 per cent of the theoretical. In nearly every case we recovered, unaltered, about one-half of the 2-methylmercapto-4-oxy-6-aminopyrimidine. Phosphorus pentachloride was used in one experiment in place of phosphorus oxychloride, but the reaction was not as smooth and more decomposition-products were formed.

*2-Methylmercapto-4,6-diaminopyrimidine,*



.—This compound has been described in a previous paper from this laboratory.[2] We prepared it by heating the above 2-methylmercapto-4-chlor-6-aminopyrimidine with concentrated aqueous ammonia, at 185°–195°, for 5 hours. When the tube was opened we obtained a colorless solution which was immediately concentrated on the steam-

[1] *Loc. cit.*

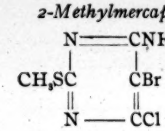
[2] Wheeler and Jamieson: *Loc. cit.*

bath. Upon cooling, a beautiful, crystalline body separated, which was purified by recrystallizing from water and alcohol. It deposited in lenticular-shaped crystals and melted at 184°–185°, to a clear oil. Analysis (Kjeldahl):

| | Calculated for $C_5H_8N_4S$. | Found. |
|---|---|---|
| N | 35.89 | 35.54 |

This mercaptodiaminopyrimidine is very stable in the presence of aqueous and alcoholic ammonia solutions. It was recovered, unaltered, after heating with concentrated aqueous ammonia, for 7 hours, at 205°–215°. It was then heated with a saturated, alcoholic solution of ammonia, for 7 hours, at 205°–215°. The pyrimidine was again recovered unaltered and melted sharply at 184°–185°.

*2-Methylmercapto-4-chlor-5-brom-6-aminopyrimidine,*



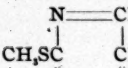
, was obtained in the form of its hydrobromic acid salt, when a molecular proportion of bromine was added to an acetic acid solution of 2-methylmercapto-4-chlor-6-aminopyrimidine. The hydrobromide sintered at about 180°–190° and then decomposed at 208°, with violent effervescence. It was purified for analysis by crystallizing from acetic acid, from which it separated, on cooling, in stout prisms. Analysis:

| | Calculated for $C_5H_4N_3SClBr_2$. | Found. |
|---|---|---|
| N | 12.51 | 12.56 |

The pyrimidine base was easily obtained from its salt by treating with a 10 per cent solution of sodium hydroxide. It was difficultly soluble in water and melted at 165°, without effervescence. The pyrimidine showed a strong tendency to occlude water. In order to thoroughly dry it for analysis it was necessary to heat for about 1 hour, at 115°–120°. Analysis:

| | Calculated for $C_5H_4N_3SClBr$. | Found. |
|---|---|---|
| N | 16.50 | 16.38 |

*2-Methylmercapto-5-brom-4,6-diaminopyrimidine,*



.—This derivative was prepared by heating 2-methylmercapto-4-chlor-5-brom-6-aminopyrimidine with aqueous ammonia, for 4 hours, at 150°–160°. When the tube was opened the compound had separated in magnificent prisms. Some of these crystals measured 3 cm. in length. The pyrimidine crystallized from hot water in beautiful prisms and melted at 192°, to a clear oil. The yield corresponded to about 80 per cent of the theoretical. Analysis (Kjeldahl):

| | Calculated for $C_5H_7N_4SBr$. | Found. |
|---|---|---|
| N | 23.83 | 23.77 |

An attempt was made to prepare this diaminopyrimidine by heating the 2-methylmercapto-4-chlor-5-brom-6-aminopyrimidine with alcoholic ammonia. After heating for 4 hours, at 150°–160°, it was recovered unaltered. The alcohol solution gave only a faint test for chlorine. The 2-methylmercapto-5-brom-4,6-diaminopyrimidine is very stable in contact with aqueous and alcoholic ammonia, at higher temperatures. After heating for 8 hours, at 180°–190°, with concentrated, aqueous ammonia, it was recovered unaltered. It was again heated with fresh aqueous ammonia, for 5 hours, at 200°–210°. Only a trace of mercaptan could be detected and the pyrimidine was recovered, melting sharply at 192°. A similar result was obtained when it was heated with concentrated, alcoholic ammonia, for 4 hours, at 200°–214°.

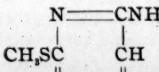
*2-Thio-4-oxy-5-brom-6-aminopyrimidine,*

was

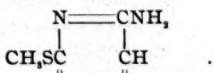
made by adding a molecular proportion of bromine to an acetic acid solution of 2-thio-4-oxy-6-aminopyrimidine. It separated from the acetic acid in granular crystals. It was difficultly soluble in acetic acid and insoluble in water. It did not melt below 300°. Analysis (Kjeldahl) :

| | Calculated for $C_4H_4ON_3SBr$. | Found. |
|---|---|---|
| N | 18.91 | 18.68 |

*2-Methylmercapto-4-anilido-6-aminopyrimidine,*



.—Four grams of 2-methylmercapto-4-chlor-6-aminopyrimidine were heated with 1 molecular proportion of aniline, for 6 hours, at 100°–130°. A clear, red varnish was obtained, which dissolved in boiling alcohol. Upon cooling, rhombic-shaped prisms separated. They were purified by recrystallizing from alcohol and melted at 121°, with violent effervescence. A nitrogen determination agreed with the calculated for a dihydrochloride :

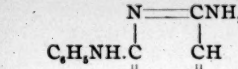


| | Calculated for $C_{11}H_{14}N_4SCl_2$. | Found. I. | Found. II. |
|---|---|---|---|
| N | 18.36 | 18.01 | 18.11 |

The free pyrimidine base was obtained by triturating the hydrochloric acid salt with an excess of dilute sodium hydroxide. The base crystallized from benzene in clusters of microscopic prisms and melted at 124°, without effervescence, to a clear oil. It gave a strong test for sulphur, but contained no chlorine. Analysis (Kjeldahl) :

| | Calculated for $C_{11}H_{13}N_4S$. | Found. |
|---|---|---|
| N | 24.13 | 23.82 |

*2,4-Dianilido-6-aminopyrimidine,*



.—Seven grams of 2-methylmercapto-4-chlor-6-aminopyrimidine were heated with 2 molecular proportions of aniline, at 140°–150°, for 10 hours. A slow effervescence took place and methylmercaptan was constantly given off. Upon cooling, the reaction-product hardened to an amorphous solid. This was treated with a warm solution of sodium hydroxide, when it melted to a heavy, thick oil. The excess of aniline was then removed by distillation with steam. On cooling, a crystalline cake remained, which weighed 10 grams. This pyrimidine was very difficult to purify. It was extremely soluble in cold alcohol, benzene and ether. It dissolved in hot water, but separated, on cooling, as an oil which finally solidified to a hard, amorphous mass. To effect purification it was converted into its sulphuric acid salt. This salt is insoluble in cold water. When warmed with water it dissociates into the free base and sulphuric acid. It can be crystallized from alcohol containing free sulphuric acid. It separated from alcohol in granular crystals and melted at 190°-193°, with effervescence. Analysis (Kjeldahl) :

| | Calculated for $C_{16}H_{15}N_5.H_2SO_4$. | Found. |
|---|---|---|
| N | 18.66 | 18.73 |

The pyrimidine base was obtained from this sulphuric acid salt by warming with a dilute solution of ammonium hydroxide. It separated as an oil, which finally solidified on standing. After drying over sulphuric acid for 24 hours, it melted at 65°–70°, to a slightly turbid oil. It is extremely soluble in the ordinary organic solvents. Analysis (Kjeldahl) :

| | Calculated for $C_{16}H_{15}N_5$. | Found. |
|---|---|---|
| N | 25.27 | 24.81 |

*2-Methylmercapto-4-parabromanilido-5-brom-6-aminopyrimidine*, $CH_3SC(N{=}CNH_2){-}CBr{=}N{-}CNHC_6H_4Br$. — The 2-methylmercapto-4-anilido-6-aminopyrimidine was dissolved in glacial acetic acid and bromine carefully added, as long as the bromine color disappeared. Stout prisms separated immediately, which were difficultly soluble in acetic acid. They decompose, with violent effervescence, at about 290°, turning somewhat brown at 210°–220°. A nitrogen determination agreed with the calculated for the hydrobromic acid salt of a dibrom-substitution-product:

| | Calculated for $C_{11}H_{11}N_4SBr_3$. | Found. |
|---|---|---|
| N | 11.89 | 12.29 |

The pyrimidine base was obtained by treating the hydrobromic acid salt with a 10 per cent solution of sodium hydroxide. It melted at 202°, without effervescence, to a clear oil. A nitrogen determination agreed with the calculated for 2-methylmercapto-4-bromanilido-5-brom-6-aminopyrimidine:

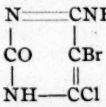
| | Calculated for $C_{11}H_{10}N_4SBr_2$. | Found. |
|---|---|---|
| N | 14.36 | 14.80 |

In order to establish the structure of this dibrompyrimidine derivative we have prepared it in the following manner: 3.6 grams of 2-methylmercapto-4-chlor-5-brom-6-aminopyrimidine were heated with 2.4 grams of parabromaniline, for 4 hours, at 120°–130°. A violet-colored oil was obtained which solidified on cooling. The material was insoluble in water, but soluble in hot acetic acid. In order to obtain the free base the substance was triturated with sodium hydroxide, filtered and then boiled in acetic acid, with animal charcoal, to remove the color. On cooling, long, slender prisms were obtained, which melted, without effervescence, at 202°. When some of this base was mixed with the above product, obtained by brominating 2-methylmercapto-4-anilido-6-aminopyrimidine (m. p.

202°), the melting-point was not lowered. Analysis (Kjeldahl):

| | Calculated for $C_{11}H_{10}N_4SBr_2$. | Found. |
|---|---|---|
| N | 14.36 | 14.31 |

*2-Oxy-4-chlor-5-brom-6-aminopyrimidine,*



This compound was obtained, in the form of its hydrobromic acid salt, when 2-oxy-4-chlor-6-aminopyrimidine was suspended in glacial acetic acid and treated with 1 molecular proportion of bromine. The hydrobromide separated as an orange-colored powder, which decomposed at 230°–240°, with effervescence. In order to obtain the free base the crude salt was warmed with a solution of dilute sodium hydroxide. When the alkali solution was acidified with dilute acetic acid the base separated as a crystalline precipitate. It crystallized from hot water in clusters of microscopic prisms and showed no definite melting-point, but began to turn brown at 210° and decomposed at about 230°, with violent effervescence. Analysis:

| | Calculated for $C_4H_3ON_3ClBr$. | Found. |
|---|---|---|
| N | 18.70 | 18.68 |

*Action of Aqueous Ammonia on 2-Ethylmercapto-6-chlorpyrimidine.*

*At 140°–150°.*—After heating with aqueous ammonia, for 4 hours, at 140°–150°, the pyrimidine was recovered unaltered.

*At 185°–195°.* — The chlorpyrimidine was heated with aqueous ammonia, for 3 hours, at 185°–195°. The ammoniacal solution was then evaporated to dryness. The crystalline residue was warmed with alcohol and filtered from the undissolved ammonium chloride. The alcoholic filtrate was then evaporated to dryness and the residue again dissolved in water. The chlorine was removed by precipitating with silver sulphate, then the sulphuric acid removed with barium hy-

droxide and the excess of barium with carbon dioxide. When the solution was evaporated to dryness we obtained a crystalline base which had all the properties of 2,6-diaminopyrimidine. It was extremely soluble in water. The base was identified by means of its platinum chloride salt. Analysis :

| | Calculated for $(C_4H_5N_4)_2.H_2PtCl_6$. | Found. |
|---|---|---|
| Pt (194.8) | 30.9 | 30.5 |

*Action of Aqueous Ammonia on 2-Ethylmercapto-5-brom-6-chlorpyrimidine.*[1]

*At 140°–150°.*—When the pyrimidine was heated with aqueous ammonia, at 140°–150°, for 4 hours, it was converted, quantitatively, into 2-ethylmercapto-5-brom-6-aminopyrimidine, melting sharply at 124°–125°.

*At 185°–195°.*—After heating for 4 hours, at 160°–170° and then for 3 hours, at 185°–195°, the 2-ethylmercapto-5-brom-6-aminopyrimidine was again obtained, melting at 124°–125°.

NEW HAVEN, CONN.,
May 1, 1905.

---

Contributions from the Sheffield Laboratory of Yale University.

## CXXVI.—RESEARCHES ON PYRIMIDINES : 2-ETHYLMERCAPTO-5-AMINO-6-OXYPYRIMIDINE.

[ELEVENTH PAPER.]

BY TREAT B. JOHNSON.

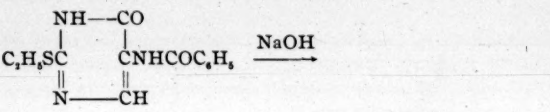
The work described in this paper was undertaken with the object of investigating the formation and properties of 2-ethylmercapto-5-amino-6-oxypyrimidine. The examination of this pyrimidine was of particular interest in the study of oxydiaminopyrimidines, because it offered the possibility of synthesizing both 2,5-diamino-6-oxypyrimidine and 2-oxy-5,6-diaminopyrimidine. The preparation of 2,5-diamino-6-oxypyrimidine from this mercaptopyrimidine will be discussed in a later paper.

In a previous paper[2] from this laboratory, it was shown that

[1] Wheeler and Johnson : *Loc. cit.*

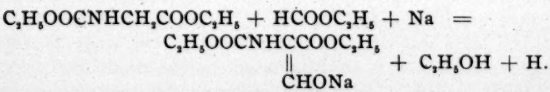
[2] Johnson and Clapp : THIS JOURNAL, 32, 131 (1904).

ethyl formate condenses, in benzene, with ethyl hippurate, in the presence of metallic sodium, to form the sodium salt of formylethylhippurate.[1] This salt condensed very readily with pseudoethylthiourea to give the benzoyl derivative of 2-ethylmercapto-5-amino-6-oxypyrimidine. Attempts to hydrolyze this acyl derivative to the free pyrimidine, (V.), were unsuccessful. Acids could not be used for the hydrolysis on account of the ease with which the mercapto radical was displaced by hydroxyl. When boiled with sodium hydroxide the pyrimidine ring was opened, to form a sodium salt of $\alpha$-benzoylamino-$\beta$-pseudoethylthioureaacrylic acid (I.). This acid was unstable and immediately condensed again to the pyrimidine, when the sodium salt was treated with acids:



I.

I now find that ethyl formate condenses very smoothly, in benzene, with carbethoxyaminoethylacetate, in the presence of metallic sodium, to form the sodium salt of formylcarbethoxyaminoethylacetate (II.):

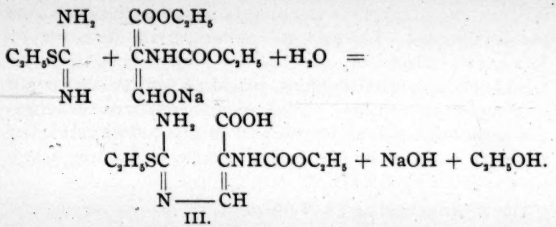


II.

This sodium salt condensed at the ordinary temperature, in aqueous solution, with pseudoethylthiourea, giving $\alpha$-carbethoxyamino-$\beta$-pseudoethylthioureaacrylic acid (III.). The yield

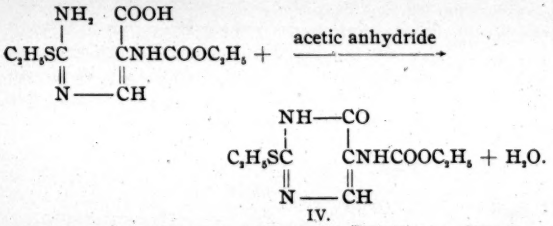
[1] Erlenmeyer, in his recent paper on the synthesis of serin and cystine, has shown that this salt can be obtained very smoothly by condensing ethyl formate with ethyl hippurate, in alcohol, by means of sodium ethylate. Ann. Chem. (Liebig), 337, 251.

of this acid corresponded to about 40–50 per cent of the theoretical :



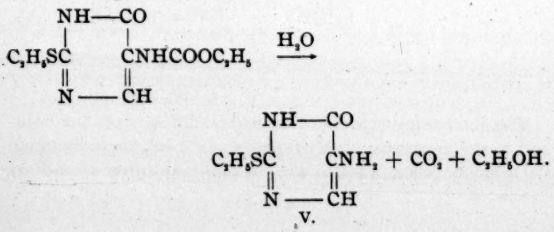
III.

In no case have I succeeded in isolating the pyrimidine—2-ethylmercapto-5-carbethoxyamino-6-oxypyrimidine, (IV.)—as a product of this condensation. This compound, nevertheless, was easily obtained when the acrylic acid was warmed with acetic anhydride.



IV.

When this pyrimidine, (IV.) was boiled with a solution of sodium hydroxide, it was converted into 2-ethylmercapto-5-amino-6-oxypyrimidine, (V.) :

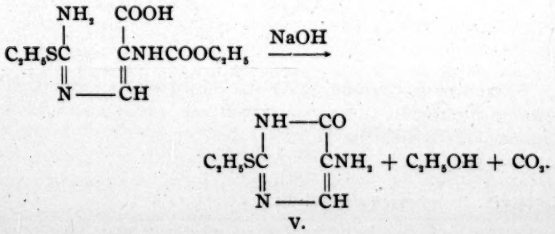


V.

The formation of the above acrylic acid, (III.) is of interest as the second case in which the formation of intermediate products has been observed in the preparation of pyrimidines from pseudothioureas. The first case observed was described by Johnson and Clapp,[1] in a paper on the preparation of 2-amino-5-methyl-6-oxypyrimidine from guanidine and the sodium salt of formylethylpropionate. They not only observed the formation of an intermediate acrylic acid in this condensation, but also were able to show that it was capable of existing in two stereoisomeric modifications.

The $\alpha$-carbethoxyamino-$\beta$-pseudoethylthiourea acrylic acid (III.) is especially characterized by its stability towards cold alkali solutions. On account of this pronounced stability I have designated it as the *trans*-modification. Under the experimental conditions I used I did not succeed in isolating an unstable *cis*-modification.

The *trans*-acid is very easily decomposed when boiled with strong and dilute solutions of sodium hydroxide. When it was boiled for a few minutes, with a strong sodium hydroxide solution and the solution then neutralized with acids or carbon dioxide, it was converted, almost quantitatively, into 2-ethylmercapto-5-amino-6-oxypyrimidine (V.):

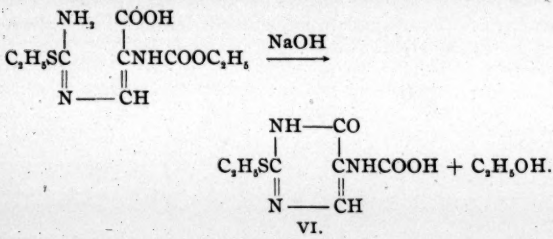


V.

This interesting saponification and condensation of the *trans*-acid to the mercaptoaminopyrimidine, (V.) led me to examine its behavior when warmed with a dilute solution of sodium

[1] *Loc. cit.*

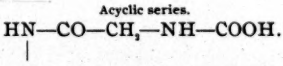
hydroxide. The experimental data at hand seem to indicate that the *trans*-acid is saponified by dilute alkali to an intermediate 2-ethylmercapto-5-carboxylamino-6-oxypyrimidine, (VI.).



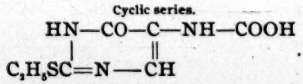
VI.

The existence of this intermediate carbamic acid is particularly interesting because of the fact that it contains a cyclic polypeptide linking. Analogous acids in the acyclic series have been obtained by Fisher,[1] in his important researches on polypeptides. The relationship between the above pyrimidine, (VI.) and a true polypeptide linking is made evident by the following comparison :

Acyclic series.



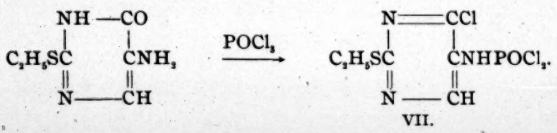
Cyclic series.



It has been the usual experience, during the investigation of pyrimidines in this laboratory, to find that a mercaptooxypyrimidine reacts normally with phosphorus oxychloride, or phosphorus pentachloride, to give a chlorpyrimidine derivative. It has also been observed repeatedly that the resulting chlorpyrimidines are obtained combined with phosphorus oxychloride. These phosphorus compounds are very unstable and

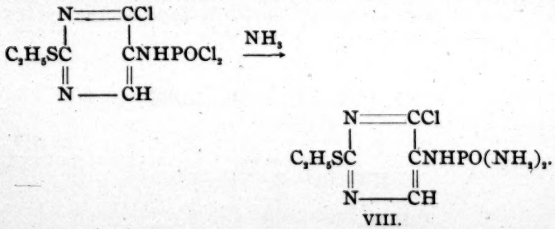
[1] Ber. d. chem. Ges., 36, 2094 (1903).

are decomposed by water, with formation of the free chlorpyrimidine. I now find that 2-ethylmercapto-5-amino-6-oxypyrimidine reacts with phosphorus oxychloride to form a phosphorus compound which is abnormally stable. The analytical determinations agree with the calculated for a phosphoryldichloride derivative (VII.):



VII.

This phosphorus derivative could be warmed with water without decomposition. When it was heated with alcoholic ammonia 2 chlorine atoms were removed and a stable compound was obtained, which I have, provisionally, represented as a phosphoryltriamide derivative,[1] (VIII.):



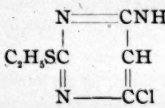
VIII.

The fact that this amino radical should show such pronounced affinity for phosphorus, is of interest. In a recent communication from this laboratory[2] it has been shown that the isomeric 2-ethylmercapto-4-oxy-6-aminopyrimidine reacts perfectly normally with phosphorus oxychloride, to form 2-ethylmercapto-4-chlor-6-aminopyrimidine, (IX.). Furthermore, Gabriel and

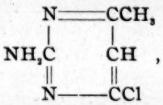
[1] These phosphoryl pyrimidine derivatives will receive further attention in this laboratory.

[2] Johnson and Johns: Preceding paper.

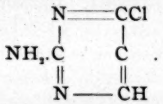
Colman[1] have shown that 2-amino-4-oxy-6-methylpyrimidine is converted, by phosphorus oxychloride, into 2-amino-4-chlor-6-methylpyrimidine. Later,[2] they observed that 2-amino-6-oxypyrimidine (isocytosine) also reacts normally with phosphorus oxychloride, to give 2-amino-6-chlorpyrimidine, (XI.).



IX.

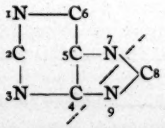


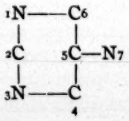
X.



XI.

In a previous publication on "Die Nucleinsaure des Weisenembryos," Osborne and Harris[3] have produced evidence to show that, in triticonucleic acid, there is a direct union between phosphorus and the nitrogen of the purine bases. Burian,[4] in a recent publication, has produced more evidence that supports the fact of this union in the nucleic acid molecule. Furthermore, his experiments tend to show that it is the nitrogen atom occupying position 7 in the purine molecule that is probably joined to the phosphorus. It is of interest to note, in this connection, that the nitrogen atom in the aminopyrimidine, (V.) which shows such affinity for phosphorus, corresponds to the nitrogen atom occupying position 7 in the purine molecule.





## EXPERIMENTAL.

*Sodium Salt of Formylcarbethoxyaminoethylacetate*, $C_2H_5OOCNHC:(CHONa)COOC_2H_5$.—The carbethoxyaminoethylacetate, used for the preparation of this sodium salt, was

[1] Ber. d. chem. Ges., **32**, 2921.
[2] *Ibid.*, **36**, 3383.
[3] Z. physiol. Chem., **36**, 85 (1902).
[4] Ber. d. chem. Ges., **37**, 708.

prepared by Fisher's[1] method, from the hydrochloride of aminoethylacetate and chlorethylformate. The hydrochloride of aminoethylacetate was prepared according to Klages'[2] directions, from methyleneaminoacetonitrile. The method is extremely suitable for preparing large quantities of this hydrochloride. Ethyl formate condenses very smoothly with carbethoxyaminoethylacetate, in the presence of sodium, in either benzene or ether; but it has been my experience that the condensation is much smoother and more rapid when benzene is used as the diluent. This sodium salt is much more stable in contact with the air than the sodium salt of formylethylacetate. I also found that the condensation could safely be accelerated by gently warming the benzene solution on the steam-bath. The purity of the salt obtained was not affected by this treatment. In all my condensations the yield of crude sodium salt has been about equal to the weight of carbethoxyaminoethylacetate used.

*Trans-α-carbethoxyamino-β-pseudoethylthiourea Acrylic Acid.*

$$\begin{matrix} C_2H_5OOC.NH—C—COOH \\ \| \\ H_2N.(C_2H_5S)C=N—CH \end{matrix}$$

.—Twenty-five grams of the sodium salt of formylcarbethoxyaminoethylacetate were dissolved in water and added to an aqueous solution of pseudoethylthiourea, which was previously prepared by treating 17 grams of pseudoethylthiourea hydrobromide with 6 grams of potassium hydroxide. The clear solution, which resulted, was then allowed to stand for a few hours, at the ordinary temperature. Upon neutralizing with acetic acid a beautiful, white, crystalline compound separated. It was insoluble in alcohol and cold water. It could be dissolved, repeatedly, in cold solutions of sodium hydroxide and be precipitated, unaltered, by acids. It was purified for analysis by recrystallizing from hot water. It separated as a colorless powder, consisting of microscopic prisms. It showed no sharp melting-point but decomposed, with effervescence, at 259°. A yield of 11.5 grams of crude material was obtained. For analysis it was dried at 100°.

[1] Ber. d. chem. Ges., **36**, 2107.
[2] *Ibid.*, **36**, 1508.

0.1574 gram substance gave 0.1341 gram $BaSO_4$ (Carius).

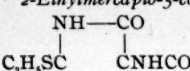
| | Calculated for $C_9H_{18}O_4N_2S$. | Found. |
|---|---|---|
| N | 16.00 | 15.75 |
| S | 12.25 | 11.70 |

The following table is given to show the comparative yields obtained in four different preparations of this *trans*-acid :

*Table.*

| Weight of carbethoxyaminoethylacetate used. Grams. | Weight of sodium salt of condensation-product. Grams. | Weight of *trans*-acid. Grams. | Percentage of theoretical. Per cent. |
|---|---|---|---|
| 30 | 32 | 11.0 | 40 |
| 20 | 25 | 11.5 | 46 |
| 40 | 45 | 20.0 | 45 |
| 40 | 45 | 19.5 | 44 |

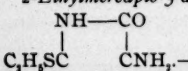
*2-Ethylmercapto-5-carbethoxyamino-6-oxypyrimidine,*



.—This compound was easily obtained when the *trans*-acid, above described, was dissolved in warm acetic anhydride. On adding water the pyrimidine separated in prisms. It was easily purified by recrystallizing from 15 per cent acetic acid and separated, on cooling, in well-developed prisms, which melted, without effervescence, at 189°-190°, to a clear oil. The pyrimidine dissolves in sodium hydroxide solution and is reprecipitated, unaltered, by acids. It was also obtained, in an impure condition, when the *trans*-acid was boiled with glacial acetic acid. Analysis :

| | Calculated for $C_9H_{18}O_3N_2S$. | Found. |
|---|---|---|
| N | 17.28 | 17.35 |

*2-Ethylmercapto-5-amino-6-oxypyrimidine,*



.—Ten grams of the *trans*-acid were dissolved in 50 cc. of water, containing 5 grams of sodium hydrox-

ide. The alkaline solution was boiled for about 20 minutes and then allowed to stand for 30 minutes. When the alkaline solution was made slightly acid with acetic acid the pyrimidine separated in beautiful, needle-like crystals, which melted, to a clear oil, at about 155°. It was purified by recrystallizing from hot water. It separated in clusters of radiating needles and, without effervescence, melted at 160°, to a clear oil. The yield was practically quantitative. This pyrimidine was also formed when 2-ethylmercapto-5-carbethoxyamino-6-oxypyrimidine was boiled with sodium hydroxide. Analysis (Kjeldahl):

| | Calculated for $C_6H_9ON_3S$. | Found. |
|---|---|---|
| N | 24.56 | 24.34 |

*Disilver Salt of 2-Ethylmercapto-5-carboxylamino-6-oxypyrimidine*, $C_7H_8SC(N{=}CCOAg)(CNHCOOAg)(N{-}CH)$.—The acid of this salt was obtained, in solution, from two different preparations of the *trans*-acid. It was formed by boiling the latter with a dilute solution of sodium hydroxide. It was very soluble in water and was not precipitated from the alkali solution by mineral acids or carbon dioxide. The disilver salt was obtained, after acidifying the alkaline solution with nitric acid, by adding a slight excess of 20 per cent silver nitrate solution. The salt was difficultly soluble in water and showed no crystalline form. Analysis of the substance, thoroughly dried over sulphuric acid:

0.1399 gram silver salt gave 0.0707 gram metallic silver.

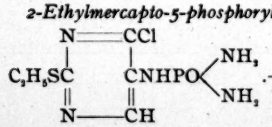
| | Calculated for $C_7H_3O_3N_3SAg_2$. | Found. |
|---|---|---|
| Ag | 50.35 | 50.53 |

*2-Ethylmercapto-5-phosphoryldichloramino-6-chlorpyrimidine*, $C_7H_8SC(N{=}CCl)(CNH.POCl_2)(N{-}CH)$.—Four and eight-tenths grams of

2-ethylmercapto-5-amino-6-oxypyrimidine were warmed, on a sand-bath, with an excess of phosphorus oxychloride. A reaction set in at once, with evolution of hydrochloric acid gas. After this ceased the excess of phosphorus oxychloride was removed by distillation under diminished pressure. I obtained a yellow, amorphous residue. When this was treated with water very little heat was evolved and a yellow, crystalline deposit remained suspended in the water. This residue was filtered and then warmed with water on the steam-bath, to destroy any phosphorus oxychloride. A thick, oily product, insoluble in water, was obtained by this treatment; it immediately solidified, on cooling, to a hard, crystalline cake. It was insoluble in the ordinary organic solvents and also in ammonium hydroxide. When treated with a solution of sodium hydroxide it showed a very peculiar behavior. The product was insoluble in sodium hydroxide, but gradually underwent decomposition and the solution assumed a dark green color. It gave strong tests for sulphur and phosphorus. It had no sharp melting-point, but decomposed at about 247°–250°. Analysis :

| | Calculated for $C_6H_7ON_3SCl_2P$. | Found. |
|---|---|---|
| N | 13.70 | 13.41 |

*2-Ethylmercapto-5-phosphoryltriamino-6-chlorpyrimidine,*



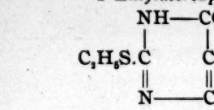
.—This complicated derivative was obtained when the above chloride was heated with alcoholic ammonia, for 3 hours, at 160°–165°. When the tube was opened there was no pressure and only a slight odor of mercaptan was noticeable. The pyrimidine was suspended in the alcohol and had a green, metallic appearance. It was insoluble in water and the ordinary organic solvents. It gave strong tests for chlorine, sulphur and phosphorus. It had no characteristic melting-point, but began to sinter at about 258° and decomposed at 290°–300°, according to the rate of heating. Analysis :

| | Calculated for $C_6H_{11}ON_3SClP$. | Found. |
|---|---|---|
| N | 26.16 | 26.12 |

*Sodium Salt of α-Benzoylamino-β-pseudoethylthiourea Acrylic Acid,* $H_2N(C_2H_5S)C : NCH : C(NHCOC_6H_5)COONa$.—This salt was obtained when 2-ethylmercapto-5-benzoylamino-6-oxypyrimidine[1] was boiled with a solution of sodium hydroxide. The sodium salt separated, on cooling, in needles. It crystallized from alcohol in needles and melted, with effervescence, at 124°–125°. When treated with acids it was converted into the unaltered pyrimidine, melting at 239°. Analysis .

| | Calculated for $C_{13}H_{14}O_5N_3S.Na.H_2O$. | Found. |
|---|---|---|
| N | 12.61 | 12.45 |

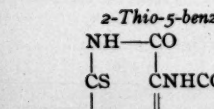
*2-Ethylmercapto-5-benzalamino-6-oxypyrimidine,*



$C_2H_5S.C : CN : CHC_6H_5$.—One gram of 2-ethylmercapto-5-amino-6-oxypyrimidine was warmed with 1 molecular proportion of benzaldehyde, for 1–2 hours, at 160°–180°. Water was given off immediately on warming and the material solidified to a crust in the hot bath. The pyrimidine crystallized from alcohol as a microscopic powder, from benzene in beautiful, rhombic plates or flattened prisms, melting at 185°–187°, to a clear oil. By prolonged boiling with water or dilute alcohol it was slowly decomposed into benzaldehyde and the unaltered pyrimidine. Analysis :

| | Calculated for $C_{13}H_{13}ON_3S$. | Found. |
|---|---|---|
| N | 16.21 | 16.00 |

*2-Thio-5-benzoylamino-6-oxypyrimidine,*

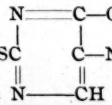


$CSCNHCOC_6H_5$.—Two grams of thiourea and 10 grams

[1] Johnson and Clapp : *Loc. cit.*

of the sodium salt of formylethylhippurate[1] were dissolved in 50 cc. of water and warmed, on the steam-bath, for about 20 minutes. The solution assumed, at once, a turbid appearance, due to the separation of ethylhippurate. Upon cooling, a small amount of crystalline material separated from the alkaline liquid. This was removed by filtration and dried on the oven. No further precipitate was obtained when the alkaline solution was acidified with acetic acid. The crystalline product was purified by crystallizing from acetic acid. It separated in plates and decomposed at 300°–310°, according to the rate of heating. It was soluble in sodium hydroxide and was reprecipitated, unaltered, by acids. It was insoluble in water and alcohol. When it was boiled with hydrochloric acid it was decomposed with evolution of hydrogen sulphide. Analysis (Kjeldahl):

| | Calculated for $C_{11}H_9O_2N_3S$. | Found. |
|---|---|---|
| N | 17.00 | 16.86 |

*2-Ethylmercapto-5,6-(μ-phenyloxazoline)pyrimidine* (By S. H. Clapp),  . — Nine grams of 2-ethylmercapto-5-benzoylamino-6-oxypyrimidine[1] were heated to boiling with 50 cc. of phosphorus oxychloride, for 3 hours. Hydrochloric acid was evolved continuously. The excess of phosphorus oxychloride was then distilled off under diminished pressure. I obtained a thick varnish, which would not solidify. This was treated with cold water, to destroy any excess of phosphorus oxychloride. Heat was evolved and a white, crystalline solid separated. This was thoroughly washed with water and purified by recrystallizing from alcohol. It melted, without effervescence, at 108°–109° to a clear oil. It was free from chlorine. Analysis (Carius):

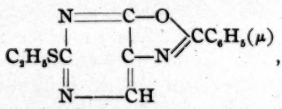
0.1399 gram substance gave 0.1268 gram $BaSO_4$.

[1] Johnson and Clapp: *Loc. cit.*

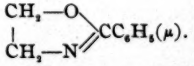
| | Calculated for $C_{18}H_{11}N_3OS$. | Found. |
|---|---|---|
| S | 12.45 | 12.43 |

The compound was insoluble in sodium hydroxide and could be boiled with alkali without decomposition. When warmed for a short time with hydrochloric acid it was converted into the unaltered 2-ethylmercapto-5-benzoylamino-6-oxypyrimidine, melting at 238°–239°. When it was suspended in dry benzene and the benzene saturated with dry hydrochloric acid gas, the hydrochloride was formed, melting, with violent effervescence, at 147°. When this salt was warmed with water it underwent dissociation and the oxazoline was recovered. Some of the hydrochloric acid salt was heated in a sealed tube, with alcoholic ammonia, for 2 hours, at 100°–110°. The alcoholic solution was evaporated to dryness and then treated with water, to remove ammonium chloride. The insoluble residue proved to be the unaltered oxazoline, melting at 108°–109°.

The close relationship between our oxazoline and $\mu$-phenyloxazoline, which was prepared by Gabriel and Heyman,[1] is shown by the following formulæ:



,



.

NEW HAVEN, CONN.,
May 6, 1905.

---

Contributions from the Chemical Laboratory of Harvard College.

## THE DETERMINATION OF PHOSPHORIC ACID BY MEANS OF AMMONIUM PHOSPHOMOLYBDATE.

[SECOND PAPER.]

BY GREGORY PAUL BAXTER AND ROGER CASTLE GRIFFIN.

In a previous paper by one of us,[2] it was shown that the precipitate, formed by adding a solution of phosphoric acid to

[1] Ber. d. chem. Ges., 23, 2495.
[2] Baxter: THIS JOURNAL, 28, 298 (1902).

a solution of an excess of molybdic acid, never possesses the formula usually assigned to it, $(NH_4)_3PO_4 12MoO_3$, but that, when washed with a solution of ammonium nitrate and heated to 300°, it always contains a greater or less excess of $MoO_3$ over that required by the above formula, owing to occlusion of either molybdic acid or ammonium molybdate. The extent of this occlusion was found, however, to be constant under given conditions of precipitation, so that the weight of the precipitate may be used for the estimation of phosphoric acid, provided the formulæ of the precipitates formed under various conditions are known. Finally, the compositions of precipitates formed in the presence of varying amounts of molybdic acid and ammonium nitrate were given.

In the first investigation, the extent of the occlusion was found to increase with increasing concentration of ammonium salts and with decreasing acid concentration, hence the conclusion was drawn that the substance occluded is ammonium molybdate and not molybdic acid. Since the Pemberton method for the determination of phosphoric acid involves the titration of ammonium phosphomolybdate with standard alkali, it is of considerable importance to obtain more conclusive evidence as to the nature of the occluded substance. Such evidence is presented in this paper and the fact is established that both ammonium molybdate and molybdic acid are occluded, the latter in larger quantities under the usual conditions of precipitation.

Since it was not determined, in the earlier investigation, whether precipitates formed in hot solutions, or by pouring molybdic acid solutions into phosphate solutions, were of the same composition as those obtained by adding phosphoric acid to molybdic acid in the cold, these points were considered first.

A solution of disodium phosphate was prepared of such a strength that 50 cc. contained about 0.1 gram of $P_2O_5$. This solution was then analyzed, according to the method described in the above-mentioned paper, as follows: Portions of exactly 50 cc. of the phosphate were poured, with constant stirring, into 100 cc. portions of the standard molybdic solution.[1]

[1] *Loc. cit.*, p. 300.

The precipitates were allowed to stand about 18 hours and then, after washing with a 10 per cent solution of ammonium nitrate, they were collected upon weighed Gooch crucibles. Finally, they were heated in an electric air-bath, at 300°–315°, for 2 hours and weighed. At this temperature the adhering ammonium nitrate is completely decomposed and constant weight attained. Precipitates formed in this way have been shown to contain 3.742 per cent of $P_2O_5$.[1] As a check upon the accuracy of these experiments, two analyses were made in which 10 grams of ammonium nitrate were added to the molybdic acid solution before precipitation and two where 200 cc. of molybdic acid were employed. The precipitates, in these cases, contained 3.739 and 8.728 per cent of $P_2O_5$, respectively.[2]

*Table I.*

| Number of analysis. | Molybdic acid. cc. | Ammonium nitrate. Grams. | Weight of precipitate. Grams. | Weight of $P_2O_5$. Gram. |
|---|---|---|---|---|
| 1 | 100 | | 2.6655 | 0.09974 |
| 2 | " | | 2.6614 | 0.09959 |
| 3 | " | | 2.6648 | 0.09972 |
| 4 | " | | 2.6626 | 0.09964 |
| 5 | " | 10 | 2.6662 | 0.09969 |
| 6 | " | 10 | 2.6631 | 0.09958 |
| 7 | 200 | | 2.6723 | 0.09960 |
| 8 | " | | 2.6724 | 0.09960 |
| | | | Average, | 0.09965 |

If precipitation is carried out in the reverse fashion, by pouring the molybdic acid into the phosphate, either inclusion or occlusion of the phosphate by the phosphomolybdate might be expected, with the result that the weight of the precipitate would be considerably too small. Furthermore, the composition of the precipitate, formed under these conditions, might be different from that of the compound produced when the phosphate is added to the molybdic acid. In analyses 9 to 12 the molybdic acid was added rapidly, with vigorous stirring, to the phosphate. The precipitates, when treated as before, varied in weight considerably, as might be expected, but

[1] *Loc. cit.*, p. 303.
[2] *Ibid.*, p. 314.

weighed slightly more, instead of less than those obtained by the reverse fashion of precipitation. To determine whether the rate of precipitation had any influence upon the weight of the precipitate, in analyses 13 to 15 the molybdic acid was added, very slowly, from a large thistle tube with a capillary outlet. The results of these experiments were not materially different from those of rapid precipitation.

A repetition of these analyses, with 200 cc. of molybdic acid and in the presence of much ammonium nitrate, gave similar results. Evidently precipitates formed by adding molybdic acid to phosphoric acid solutions are too variable in composition to be suitable for exact quantitative work.

*Table II.*

| Number of analysis. | Molybdic acid. | Ammonium nitrate. | Rate of precipitation. | Weight of precipitate. | Calculated weight of precipitate. | Difference. |
|---|---|---|---|---|---|---|
| | cc. | Grams. | | Grams. | Grams. | Gram. |
| 9 | 100 | | Rapid | 2.6754 | 2.663 | 0.012 |
| 10 | " | | " | 2.6678 | " | 0.005 |
| 11 | " | | " | 2.6630 | " | 0.000 |
| 12 | " | | " | 2.6660 | " | 0.003 |
| 13 | " | | Slow | 2.6615 | " | —0.001 |
| 14 | " | | " | 2.6689 | " | 0.006 |
| 15 | " | | " | 2.6762 | " | 0.013 |
| 16 | 200 | | Rapid | 2.6768 | 2.673 | 0.004 |
| 17 | " | | " | 2.6898 | " | 0.017 |
| 18 | " | | " | 2.6758 | " | 0.003 |
| 19 | " | | Slow | 2.6705 | " | —0.002 |
| 20 | " | | " | 2.6785 | " | 0.006 |
| 21 | 100 | 10 | Rapid | 2.6721 | 2.665 | 0.007 |
| 22 | " | 10 | " | 2.6659 | " | 0.001 |
| 23 | 200 | 10 | " | 2.6700 | 2.677 | —0.007 |

It may be added that all the precipitates formed by pouring the molybdic acid into the phosphate showed a much greater tendency to adhere tenaciously to the beaker than those precipitated in the reverse fashion. Several analyses were lost through inability to remove the precipitate from the glass even by the most vigorous rubbing with a rubber "policeman."

The usual directions for the determination of phosphoric acid with molybdic acid advocate precipitation in warm solution, for precipitation in warm or hot solution is completed more rapidly than in cold solution and, furthermore, has the advantage that the precipitate is more highly crystalline and, therefore, may be more easily manipulated. To determine whether the composition of the precipitate is affected by the temperature, experiments were carried out as follows: In analyses 24 and 25 both molybdic acid and phosphate were heated to 50° and then the phosphate was added to the molybdic acid. The precipitates were maintained at 50°–60° for nearly 4 hours and were then washed with ammonium nitrate and collected. In one experiment, where filtration took place after only 1½ hours, precipitation was incomplete. In analysis 26 precipitation took place at room temperature and the precipitate was digested for nearly 4 hours, at 50°–60°.

*Table III.*

| Number of analysis. | Molybdic acid. | Weight of precipitate. | Calculated weight of precipitate. | Difference. |
|---|---|---|---|---|
| | cc. | Grams. | Grams. | Gram. |
| 24 | 100 | 2.6890 | 2.663 | 0.023 |
| 25 | 200 | 2.7019 | 2.673 | 0.029 |
| 26 | 100 | 2.6765 | 2.663 | 0.014 |

All three results show that the extent of the occlusion is greater at high temperatures than at low and analysis 26 indicates that occlusion may take place after precipitation, as was pointed out in the previous paper.[1] Since the occlusion probably varies considerably with the temperature and period of heating, high temperatures should be avoided in the precipitation of ammonium phosphomolybdate, if the precipitate is to be weighed.

The question as to whether ammonium phosphomolybdate occludes molybdic acid or ammonium molybdate was somewhat difficult to settle. Since, as has already been said, the extent of the occlusion increases with increasing concentration of ammonium salts and with diminishing acid concentration, it seems probable that ammonium molybdate and not molybdic acid is carried down. Much more conclusive evidence, how-

[1] *Loc. cit.*, p. 312.

ever, would be afforded by a direct determination of either the free molybdic acid or the ammonia in the precipitate.

At first the attempt was made to determine the free molybdic acid by dissolving the precipitate in half-normal potassium hydroxide and titrating the excess of alkali with standard acid, in the presence of phenolphthalein. The precipitate was not ignited before the titration, since the occluded substance, whether ammonium molybdate or molybdic acid, is converted into molybdic trioxide at 300°. Qualitatively this method was successful, although the end-point with phenolphthalein, in the presence of ammonia, is not at all sharp.

Fifty cc. portions of a sodium phosphate solution, containing 0.1018 gram of phosphorus pentoxide, were precipitated by addition to 100 cc. and 200 cc. portions of molybdic acid. The precipitates were allowed to stand some time and then were washed thoroughly, by decantation, with a 5 per cent solution of ammonium nitrate and were freed, as far as possible, from the washing solution by suction upon a Gooch crucible. Next the precipitates were transferred with water to beakers, dissolved in a slight excess of half-normal potassium hydroxide, which had been freed from carbonate by means of a slight excess of barium hydroxide and, finally, the excess of hydroxide was determined by titration with standard acid, in the presence of phenolphthalein. Since all the precipitates contained exactly the same amount of phosphorus pentoxide, the slightly larger volumes of alkali required by the precipitates obtained with 200 cc. of molybdic acid point to the presence of more occluded molybdic acid in these precipitates than in those formed with 100 cc. of molybdic acid. It is noticeable also that the quantities of hydroxide used correspond much more nearly to the requirement of 48 molecules of potassium hydroxide than to that of 46 molecules, for each molecule of phosphorus pentoxide. Assuming that, in the titration, the neutral point with phenolphthalein is reached when the neutral molybdate and the dimetallic phosphate have been produced, the formula of the precipitate must be

$(NH_4)_3HPO_4 12MoO_3$ and not. $(NH_4)_3PO_4 12MoO_3$,

as is usually assumed.

*Table IV.*

| Number of analysis. | Molybdic acid. | Weight of $P_2O_5$. | N/2 KOH used. | Theory for 46 molecules KOH. | Theory for 48 molecules KOH. |
|---|---|---|---|---|---|
| | cc. | Gram. | cc. | cc. | cc. |
| 27 | 100 | 0.1018 | 67.81 | 65.97 | 68.94 |
| 28 | " | " | 68.40 | " | " |
| 29 | 200 | " | 68.65 | " | " |
| 30 | " | " | 68.27 | " | " |

In order to avoid the uncertainty of the phenolphthalein end-point, an attempt was made to perform the titrations with methyl orange, by first removing the weak phosphoric and molybdic acids with barium chloride, after solution of the phosphomolybdate in standard alkali. Although, as in the previous experiments, it was evident that more alkali was required for precipitates formed with a large excess of molybdic acid than with a small excess, no more satisfactory quantitative results were obtained than in the previous case, owing, apparently, to the fact that the precipitated barium phosphate and molybdate were not of constant composition.

Attention was next turned to the more promising problem of the determination of the ammonia in the precipitate. If the occluded substance is molybdic acid, the relation of the ammonia to the phosphorus pentoxide should be constant under all conditions of precipitation, while, if ammonium molybdate is occluded, the ratio of ammonia to phosphoric acid will increase with increasing occlusion. Obviously, a washing solution must be obtained which contains no ammonium salts. Since water decomposes the precipitate and since nitric acid dissolves it appreciably, potassium nitrate was first chosen for the purpose. In order to show that ammonium phosphomolybdate is not appreciably soluble in this medium, several precipitates, formed in the usual way, were washed with a 10 per cent solution of potassium nitrate. When the washings were treated with a large excess of molybdic acid, they remained perfectly clear and colorless. Moreover, when these precipi-

tates were further washed with 10 per cent ammonium nitrate solution, collected and weighed, they were almost absolutely identical in weight with those where the potassium nitrate treatment was omitted.

*Table V.*

| Number of analysis. | Molybdic acid. cc. | Weight of precipitate. Grams. | Calculated weight of precipitate. Grams. |
|---|---|---|---|
| 31 | 100 | 2.6715 | 2.676 |
| 32 | " | 2.6787 | " |
| 33 | " | 2.6732 | " |

The per cent of ammonia in precipitates formed in the usual way was determined as follows: They were first washed with 10 per cent potassium nitrate solution and collected upon Gooch crucibles. Then they were transferred to a retort with water. By means of a rubber stopper a dropping funnel was fitted to the tubulature of the retort, through which concentrated potassium hydroxide was introduced. Finally, the ammonia was distilled into N/10 hydrochloric acid. A very small negative correction was necessary on account of the use of rubber in the distilling apparatus. This correction was determined by blank experiments:

*Table VI.*

| Number of analysis. | Weight of precipitate calculated. Grams. | Weight of $P_2O_5$ calculated. Gram. | N/10 HCl used. cc. | Per cent of ammonia. | Molecules of ammonia for 1 molecule of $P_2O_5$. |
|---|---|---|---|---|---|
| 34 | 2.676 | 0.1001 | 11.80 | 0.752 | 1.67 |
| 35 | " | " | 13.02 | 0.830 | 1.84 |
| 36 | " | " | 10.43 | 0.665 | 1.48 |

It was evident that either ammonium phosphomolybdate contains very much less ammonium than is usually supposed, or else the ammonium in the precipitate had been replaced by the potassium of the washing solution. The latter explanation proved to be the correct one, for in an experiment where a similar precipitate was washed with potassium nitrate and

then allowed to stand in contact with potassium nitrate for about a day, the per cent of ammonia was found to be 0.44, which corresponds to 0.98 molecule of ammonia for each molecule of phosphorus pentoxide and in another, where the precipitate stood under 10 per cent potassium nitrate for 3 weeks, with occasional replacement with fresh solution, the per cent of ammonia was only 0.13, corresponding to 0.28 molecule of ammonia.

Since potassium is heavier than ammonium, it might be expected that the precipitates in analyses 31 to 33, where potassium had replaced ammonium to a considerable extent, would have been heavier than those which had been washed with ammonium nitrate only. Evidently, however, the potassium, in the presence of a high concentration of ammonium, is as easily replaced by ammonium. Hence the precipitates in question, after the final washing with ammonium nitrate to which they were subjected, contained little potassium and the results were the same as if the potassium nitrate treatment had been omitted.

A final attempt to determine the ammonia content was then made in the following way: Precipitates of the phosphomolybdate were collected upon Gooch crucibles, after being washed with 1 per cent nitric acid. Since a small portion of the precipitate was dissolved by the nitric acid, the filtrates were treated with a large amount of molybdic acid and were allowed to stand over night, to insure complete precipitation of the dissolved phosphomolybdate. The weight of this small amount of precipitate was determined and, in the calculations, was subtracted from the theoretical weight of the ignited precipitate. The main precipitate was transferred to a retort and the ammonia determined as described above. Although the dissolved phosphomolybdate was precipitated from the filtrate and washing solution in the presence of a much larger excess of molybdic acid than the main bulk of the precipitate, the weight of the dissolved substance was so small, between 0.0000 and 0.0180 gram, that the different conditions of precipitation could not have affected the weight of the whole precipitate to an extent greater than a few thousandths of a per cent.

*Table VII.*

| Number of analysis. | Molybdic acid. | Weight of precipitate calculated. | Weight of $P_2O_5$ calculated. | N/10 HCl used. | Per cent of ammonia. | Molecules of ammonia for $P_2O_5$. |
|---|---|---|---|---|---|---|
| | cc. | Grams. | Gram. | cc. | | |
| 37 | 100 | 2.7121 | 0.1015 | 29.98 | 1.881 | 4.20 |
| 38 | " | 2.6802 | 0.1003 | 29.48 | 1.872 | 4.17 |
| 39 | " | 2.7188 | 0.1017 | 30.71 | 1.922 | 4.29 |
| 40 | 200 | 2.7200 | 0.1014 | 28.78 | 1.801 | 4.03 |
| 41 | " | 2.7245 | 0.1016 | 29.89 | 1.867 | 4.18 |
| 42 | " | 2.7300 | 0.1018 | 29.86 | 1.862 | 4.17 |
| 43 | " | 2.1640 | 0.0807 | 23.11 | 1.818 | 4.07 |
| 44 | " | 2.7175 | 0.1013 | 28.44 | 1.791 | 3.99 |

Since ammonium phosphomolybdate is always precipitated in the presence of much nitric acid, it is extremely probable that its composition was not changed during the washing with dilute nitric acid. Consequently, there can be no doubt, from the above results, that in ammonium phosphomolybdate only 2 of the hydrogens of phosphoric acid are replaced by ammonium and that its formula is, approximately, $(NH_4)_2HPO_4 12MoO_3$. This is to be expected, however, from the fact that ammonia is a very weak base and phosphoric acid a very weak acid, so that the tertiary ammonium phosphate should be largely hydrolyzed in water solution and, in strongly acid solution, would be chiefly converted into molecular phosphoric acid. This conclusion is borne out by some unpublished experiments by Professor C. R. Sanger, in this laboratory, in which he found that triammonium phosphate is too unstable to be obtained in the solid state, from solution and that even the diammonium phosphate readily parts with a considerable portion of its ammonia.

In Table VII. the small excess over 4 molecules of ammonia for every molecule of phosphorus pentoxide is undoubtedly due to occluded ammonium molybdate. In the previous paper[1] it was shown that, in precipitates formed with 100 cc. of molybdic acid for 0.1 gram of phosphorus pentoxide, the excess of

[1] *Loc. cit.*, p. 305.

molybdic trioxide, over that theoretically necessary from the formula $(NH_4)_3PO_4 12MoO_3$, was 1.08 per cent, which, in the form of ammonium molybdate, corresponds to 0.52 molecule of ammonia for every molecule of phosphorus pentoxide. Evidently the occluded substance is chiefly molybdic acid, since the excess actually found is only about 0.2 of a molecule. The slightly smaller excess in the precipitates formed with the larger quantities of molybdic acid, although the precipitates themselves are heavier, indicates less occlusion of ammonium molybdate but greater occlusion of molybdic acid. Doubtless this is due to the fact that, if a small excess of molybdic acid is employed, the acidity of the solution is diminished to a much greater extent by the formation of the precipitate, owing to its strongly acid nature, than when a large excess of molybdic acid is used. If, moreover, the acid concentration should be still further diminished by the use of a lower concentration of nitric acid in the molybdic acid solution, a still larger proportion of occluded ammonium molybdate is to be expected. This expectation was fulfilled in the following experiments. Precipitates were produced with the use of a molybdic acid solution containing one-half the usual concentration of nitric acid. These were washed with nitric acid and analyzed for ammonia as before. Under these conditions more than half the occluded substance was found to be ammonium molybdate.

*Table VIII.*

| Number of analysis. | 2% Molybdic acid. | Weight of precipitate calculated. | Weight of $P_2O_5$ calculated. | N/10 HCl used. | Per cent of ammonia. | Molecules of ammonia for $P_2O_5$. |
|---|---|---|---|---|---|---|
| | cc. | Grams. | Gram. | cc. | | |
| 45 | 100 | 2.7492 | 0.1040 | 31.65 | 1.964 | 4.32 |
| 46 | " | 2.7623 | 0.1045 | 31.69 | 1.957 | 4.36 |

These results, as well as those recorded in Table VII., are in decided conflict with analyses made in the previous research, where the percentages of ammonia, in precipitates

which had been washed with ammonium nitrate and then heated to 300°, were found to be from 2.627–to 2.665, corresponding to about 6 molecules of ammonia for each molecule of phosphorus pentoxide. However, it was impossible, by suction upon Gooch crucibles, completely to free the precipitates from the ammonium nitrate solution used in the washing and, since the precipitates were then heated to 300° while still moistened with the ammonium nitrate, it is evident that during the ignition the third hydrogen of the phosphoric acid was replaced by the ammonium from this ammonium nitrate.

In order to weigh precipitates in which it was impossible that this replacement of hydrogen by ammonium could have taken place, experiments were performed with the use of 1 per cent nitric acid, instead of ammonium nitrate, as the washing solution. The precipitates were collected upon Gooch crucibles and heated to 300°, as already described. The filtrates and wash-waters were carefully preserved and the dissolved phosphomolybdate was determined as on page 212. Although the small quantity of precipitate, obtained from the filtrate and wash-waters, was of somewhat different composition from the main bulk of the precipitate, this difference could not have produced an error of more than 0.1 or 0.2 of a milligram.

*Table IX.*

| Number of analysis. | Molybdic acid. | Weight of main precipitate. | Weight of precipitate from filtrate. | Total weight of precipitate. |
|---|---|---|---|---|
| | cc. | Grams. | Gram. | Grams. |
| 47 | 100 | 2.6808 | 0.0082 | 2.6890 |
| 48 | " | 2.6757 | 0.0118 | 2.6875 |
| 49 | " | 2.6816 | 0.0091 | 2.6907 |
| | | | Average, | 2.6891 |

Precipitates prepared in exactly the same manner, but washed with ammonium nitrate, weighed, on an average, 2.7223 grams. Such precipitates have been shown to contain 1.08 per cent excess of molybdic trioxide, owing to occlusion, which corresponds to 0.286 molecule of molybdic trioxide for each molecule of phosphorus pentoxide, hence they have the formula $(NH_4)_3PO_4 12.143MoO_3$. The precipitates obtained

as those in Table IX. should, then, have the formula $(NH_4)_3HPO_4 12.143MoO_3$ and should weigh 2.698 grams, which is slightly more than that actually found. The previous conclusion, that the precipitate formed by the addition of a phosphate to a solution of molybdic acid is the diammonium phosphomolybdate is thus supported.

*Summary.*

The results of this investigation are as follows :

1. The conclusion reached in the previous paper is confirmed, that it is possible to obtain ammonium phosphomolybdate constant in composition and in a state suitable for weighing, so that it may be used for the accurate estimation of phosphoric acid.

The composition of the precipitate varies with the excess of molybdic acid, however, hence the excess of precipitant must be known. For the composition of the precipitate under different conditions the previous paper should be consulted. Attention is called to an obvious typographical error in the diagram on p. 314 of that paper, where the fourth abscissa should be 3.735 instead of 3.730.

The precipitate must be formed by pouring the phosphate into the molybdic acid. If the precipitation is performed in the reverse manner the composition of the precipitate varies considerably.

The precipitation should be performed at room temperature. At higher temperatures occlusion is increased.

2. The ammonium in the precipitate is readily replaced by potassium, in the presence of a high concentration of potassium salts, but the reverse change takes place if the potassium phosphomolybdate is then treated with concentrated ammonium salts.

3. The precipitate of ammonium phosphomolybdate is the diammonium salt.[1] When heated to a high temperature with ammonium nitrate it is converted, almost wholly, into the triammonium phosphomolybdate.

[1] Gibbs found only 5 molecules of ammonia for each molecule of phosphorus pentoxide. THIS JOURNAL, 3, 324 (1881).

4. Ammonium phosphomolybdate occludes varying amounts of both molybdic acid and ammonium molybdate, according to the conditions of precipitation.

5. The Pemberton method for the determination of phosphoric acid, by titration of ammonium phosphomolybdate with standard potassium hydroxide, is incapable of giving accurate results for several reasons. In the first place, 24 molecules of alkali are required for the neutralization of 1 molecule of ammonium phosphomolybdate and not 23, as is commonly assumed. Secondly, ammonium phosphomolybdate occludes varying amounts of molybdic acid. Finally, the titration with phenolphthalein, in the presence of ammonia, always yields uncertain results.

6. No method for estimating phosphoric acid, which depends upon the determination of the molybdic acid in ammonium phosphomolybdate, is accurate unless allowance is made for the occluded ammonium molybdate and molybdic acid.

CAMBRIDGE, MASS.,
April 26, 1905.

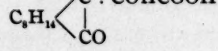
## CONDENSATION COMPOUNDS OF CAMPHOROXALIC ACID AND AMINES.

[SEVENTH COMMUNICATION ON CAMPHOROXALIC DERIVATIVES.[1]]

BY J. BISHOP TINGLE AND WILLIAM EDWIN HOFFMAN, JR.

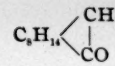
### THEORETICAL.

The investigations carried out by J. Bishop Tingle and his co-workers have shown, almost conclusively, that the condensation compound of camphor and ethyl oxalate, which has been termed camphoroxalic acid, is an unsaturated keto-alcohol,



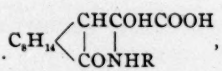
and not the 1,3-diketone,

[1] The previous papers on this subject are as follows: Inaug. Diss., Munich, 1889, p. 34. J. Chem. Soc., **57**, 652 (1890). THIS JOURNAL, **19**, 393 (1897); **20**, 318 (1898); **21**, 238 (1899); **23**, 214 (1900). J. Am. Chem. Soc., **23**, 363 (1901).

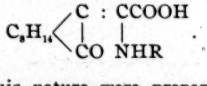


In the course of the work, a new class of compounds was discovered, formed by the condensation of the acid with amines.[1]

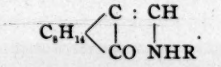
The condensation compounds of the sodium and potassium salts of camphoroxalic acid and of the ethyl ester with amines, both aliphatic and aromatic, were studied. The primary products, in all cases, were, apparently, additive substances of the general type,



but only one compound with this formula could be isolated. It was obtained from hydroxylamine and sodium camphoroxalate, the other substances appeared to be unstable and eliminated the elements of water, giving rise to products of the general formula :



Compounds of this nature were prepared from ammonia, hydroxylamine, semicarbazine, aniline and $\alpha$- and $\beta$-naphthylamine. Such substances as those formulated above might be expected to undergo further change ; carbonic anhydride might be evolved with the formation of a compound of the type :

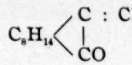


In addition to the above, a third compound of the amine with camphoroxalic acid might be formed, namely, a salt of the acid mentioned above ; this would be represented by the formula :

[1] J. Am. Chem. Soc., **23**, 363 (1901).

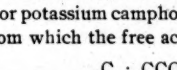
Representatives of these various types were actually prepared from aniline and sodium camphoroxalate. The first by the action of the constituents in a neutral solvent, at the ordinary temperature; the second by the action of aniline and camphoroxalic acid, under pressure, at 130°, or by heating the first compound above its melting-point. The third derivative was obtained by the action of aniline on free camphoroxalic acid, in a neutral solvent, at the ordinary temperature.

In naming these compounds the simplest and most advisable method appeared to be to regard them as derived from the complex,

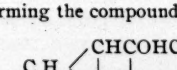


for which the term camphoformene was suggested; it is self-explanatory and indicates the presence of the double linkage.

By the action of ammonia on sodium or potassium camphoroxalate, sodium or potassium camphoformeneaminecarboxylate was obtained, from which the free acid,



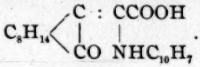
was isolated. Sodium camphoroxalate combines with hydroxylamine, forming the compound



Semicarbazine unites with potassium or sodium camphoroxalate under the same conditions as hydroxylamine. The products were thought to consist of two compounds having, apparently, the same empirical formula, but differing in their behavior toward solvents.

$\alpha$-Naphthylamine reacted with sodium camphoroxalate, un-

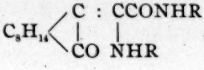
der somewhat similar conditions to aniline and formed $\alpha$-naphthylcamphoformeneaminecarboxylic acid. The corresponding derivative of $\beta$-naphthylamine was also obtained:



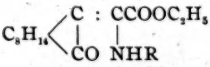
The interaction of orthophenylenediamine and sodium camphoroxalate produced camphoquinoxaline, $C_{18}H_{20}N_2O_2$.

ETHYL CAMPHOROXALATE DERIVATIVES.

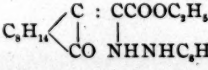
Methylamine, ethylamine, semicarbazine, aniline and ammonia condensed with ethylcamphoroxalate to form compounds of the general formula,



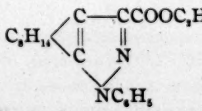
while, with aniline or $\beta$-naphthylamine, the product has the formula



Phenylhydrazine reacted with ethyl camphoroxalate forming



when this was heated above its melting-point ethyl camphylphenylpyrazolcarboxylate,

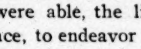


results and, on hydrolyzing this compound, the free acid was obtained.

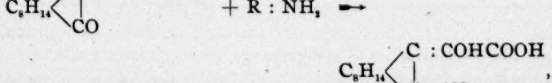
Condensation compounds could not be isolated from ethyl

camphoroxalate or sodium camphoroxalate with para- and metaphenylenediamine, ethylaniline and dimethylaniline.

The object of the present investigation was to determine, if possible, what action would take place between the free camphoroxalic acid and aliphatic and aromatic amines. To ascertain, as far as we were able, the limits within which the condensation takes place, to endeavor to find the cause of the inhibition of the reaction with some amines, whether it was due to stereometrical influences, to the aliphatic or aromatic nature of the amine, or to its more or less strongly developed positive properties and to try to discover the conditioning factors for the production of substances of the varying types referred to in the preceding pages. The action of camphoroxalic acid upon a number of metallic compounds was also investigated and the typical salts of camphoroxalic acid, described below, have been prepared and analyzed. Finally, we desired to investigate the action of acylhalides or substituted acylhalides upon compounds of the type,

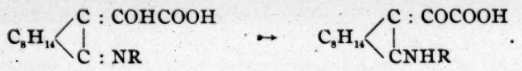


the object being to endeavor to obtain evidence of the existence, in these compounds, of the group $R_2NH$. Although the behavior of hydroxylamine and phenylhydrazine towards ethyl camphoroxalate, which has already been referred to (pp. 218, 220) makes it highly probable that the amine attacks the group $>COH$, yet the possibility of the carbonyl group of the camphor nucleus first reacting with the amine must also be recognized, this, however, would involve the following changes:



that is, the : C.OH group would remain intact and should be capable of recognition as such, but this was not found to be the

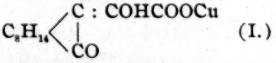
case. The alternative suggestion is that intramolecular rearrangement might take place and result in the change:



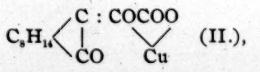
At present there is no evidence in support of this latter view, while the fact that, apart from the salt forming action of the carboxyl group, camphoroxalic acid combines with amines in equimolecular proportion would appear to be decisively against it.

## METALLIC SALTS OF CAMPHOROXALIC ACID.

When copper nitrate is allowed to react with camphoroxalic acid, in a solution of 50 per cent alcohol, at ordinary temperatures, a greenish, crystalline mass is obtained, which melts and decomposes at 275° and has the formula $C_{11}H_{14}O_4Cu$. The product is the same, irrespective of the proportions in which the copper nitrate and acid are mixed. Two views are possible of the constitution of this salt; if the copper is present in the cuprous condition, it would be



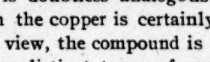
if in the cupric state, the formula



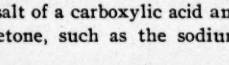
would apply and analysis could, of course, not distinguish between them. At first sight, Formula I., where the carboxyl group only is affected, would seem to be the more probable, and this view might be thought to derive support from the observation that, when the salt is heated, in alcoholic solution, at 100°, cuprous oxide is deposited. The view that the salt is represented by Formula II. is based upon the following facts: Its green color is characteristic of the cupric but not of the cuprous state. In solution the salt fails to give any indication of the presence of copper ions, which behavior is entirely in

accordance with Formula II. Moreover, unlike the barium salt described below, this one gives no coloration with ferric chloride and alcohol, indicating that a change has taken place in the : COH group of the camphoroxalic acid. The decomposition, on heating at 100°, is doubtless analogous to that of Fehling's solution, in which the copper is certainly in the cupric state. According to this view, the compound is a representative of a combination of two distinct types of organo-metallic derivatives, *viz.*, the salt of a carboxylic acid and the metallic derivative of a diketone, such as the sodium derivative of ethyl acetoacetate.

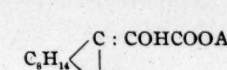
When a solution of silver nitrate, in 50 per cent alcohol, is allowed to react with camphoroxalic acid, a colorless *silver salt*,



is formed. Under similar conditions barium nitrate and camphoroxalic acid form a *barium salt*,



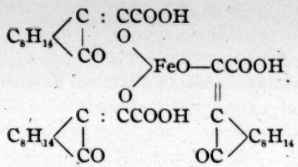
Calcium nitrate reacts in the same manner, forming the *calcium salt*,



In the case of ferric chloride and camphoroxalic acid, the compound which is formed has the characteristic, dark, reddish-violet color, which results, in general, when ferric chloride acts, in alcoholic solution, on a compound containing the enol grouping. This substance is somewhat similar to the compounds prepared by R. Schieff, in his work on acetoacetic ester when in combination with benzyl aniline.[1]

Its constitution seems to be represented by the formula

[1] Ber. d. chem. Ges., 31, 205, 601.



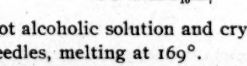
This is based on the results obtained by analysis and on the fact that the salt dissolves slowly in boiling sodium carbonate solution. It melts at about 85°.

## ACTION OF AMINES ON CAMPHOROXALIC ACID.

### 1. β-NAPHTHYLAMINE.

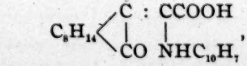
β-Naphthylamine and camphoroxalic acid yield three compounds :

1. The first of these, ***β-naphthylamine-β-naphthylcamphoformeneaminecarboxylate,***



is formed in hot alcoholic solution and crystallizes in slender, pale-yellow needles, melting at 169°.

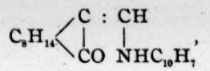
2. The second compound is obtained when this salt, in very dilute alcoholic solution, is treated with sodium hydroxide and the product acidified. ***β-Naphthylcamphoformeneaminecarboxylic acid,***



crystallizes from alcohol in slender, bright-yellow needles, melting at 172°.5. This compound has been previously described by J. Bishop Tingle and Alfred Tingle.[1]

3. The third compound from β-naphthylamine and camphoroxalic acid, ***β-naphthylcamphoformeneamine,***

[1] J. Am. Chem. Soc., **23**, 375 (1901).

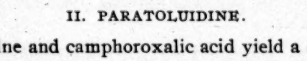


is formed by heating either of the preceding substances above its melting-point. It crystallizes in slender, pale-yellow prisms, melting at 173°.

II. PARATOLUIDINE.

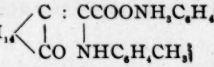
Paratoluidine and camphoroxalic acid yield a series of three compounds, corresponding to those formed by β-naphthylamine.

1. The *p-toluidine p-tolylcamphoformeneaminecarboxylate*,



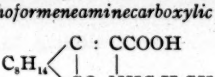
is formed in alcoholic solution and crystallizes readily from alcohol in pale-yellow needles, melting at 152°.

2. *p-Tolylcamphoformeneaminecarboxylic acid*,



is formed from the above salt by treatment with sodium hydroxide solution and subsequent acidification of the product. It crystallizes from benzene in pale-yellow prisms, melting at 168°.

3. *p-Tolylcamphoformeneamine*,

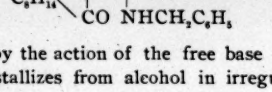


is formed by heating either of the two preceding substances above its melting-point. From alcohol it crystallizes in slender, yellow prisms, melting at 178°.

III. BENZYLAMINE.

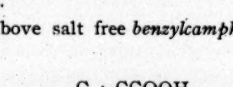
Benzylamine forms, with camphoroxalic acid, a series of three compounds, similar to those produced by β-naphthylamine and *p*-toluidine.

1. *Benzylamine benzylcamphoformeneaminecarboxylate,*



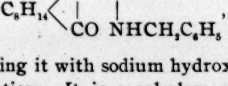
is obtained by the action of the free base on camphoroxalic acid and crystallizes from alcohol in irregular rhombohedra, melting at 174°.5.

2. From the above salt free *benzylcamphoformeneaminecarboxylic acid,*



is formed by treating it with sodium hydroxide and acidifying the resulting solution. It is a colorless compound, crystallizing from ethyl acetate in clusters of fine prisms, melting at 140°.

3. When heated above its melting-point, each of the preceding compounds decomposes, forming *benzylcamphoformeneamine,*



which, from alcohol, crystallizes in colorless prisms, melting at 96°.5.

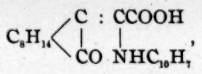
### IV. α-NAPHTHYLAMINE.

From α-naphthylamine and camphoroxalic acid two compounds are obtained; *α-naphthylamine naphthylcamphoformeneaminecarboxylate,*

is formed in alcoholic solution and, when purified by means of this solvent, yields greenish-yellow prisms, melting at 165°.

2. The above salt, when heated with sodium hydroxide

solution and the product acidified, gives *α-naphthylcamphoformeneaminecarboxylic acid*,



which crystallizes from benzene with 0.5 molecule of benzene and melts at 170°.

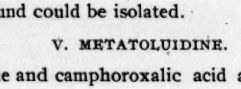
This acid has been described by J. Bishop Tingle and Alfred Tingle.[1]

3. When heated above its melting-point, each of the two preceding substances formed a viscous mass, from which no definite compound could be isolated.

### V. METATOLUIDINE.

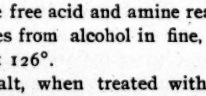
Metatoluidine and camphoroxalic acid also yield two compounds :

1. *Metatoluidine metatolylcamphoformeneaminecarboxylate*,



is formed when the free acid and amine react in alcoholic solution ; it crystallizes from alcohol in fine, pale lemon colored needles, melting at 126°.

2. The above salt, when treated with sodium hydroxide solution and the product acidified, gives *metatolylcamphoformeneaminecarboxylic acid*,



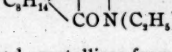
which crystallizes from benzene in colorless needles and melts at 154°. When heated above its melting-point, each of the preceding substances formed a viscous mass, from which no definite compound could be isolated.

### VI. DIETHYLAMINE.

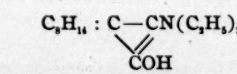
Diethylamine and camphoroxalic acid react, in alcoholic solution, to form two compounds :

[1] J. Am. Chem. Soc., **23**, 375 (1901).

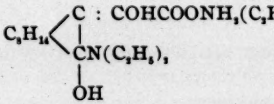
1. *Diethylamine Diethylcamphoformolaminecarboxylate,*

This compound crystallizes from alcohol in colorless needles, melting at 139°.5. It differs from the foregoing salts of camphoformeneaminecarboxylic acid in that its formation does not involve the elimination of the elements of water, in which respect it resembles the hydroxylamine derivative previously referred to (p. 218). With an alcoholic solution of ferric chloride no color reaction is produced. The term "*camphoformol*" is suggested for the complex  . It differs from "*camphoformene*" by the addition of the elements of water, one hydrogen atom being united to the camphor nucleus.

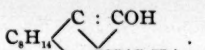
2. When this salt is heated above its melting-point it gives off water, carbonic anhydride and diethylamine and forms a compound of the same empirical formula as diethyl camphoformeneamine, $C_{18}H_{29}NO$, but which differs from what we should expect of that substance by virtue of the fact that, with ferric chloride and alcohol, it gives the reddish-violet color characteristic of the enol grouping; this seems to indicate that the reaction leading to its formation is hardly so simple as that which yields the corresponding derivatives of other amines. It may be possible that an isomeric compound,



is produced, or it may be that diethylamine and camphoroxalic acid yield, first, the hypothetical compound,



which, when heated, would doubtless give a body with the formula



This matter will be investigated at the first suitable opportunity, because the substance in question might furnish an interesting case of dynamic isomerism.

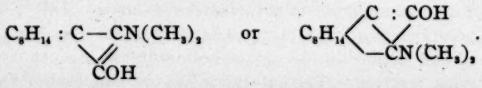
The compound crystallizes from ethyl acetate in colorless needles, melting at 153°.

### VII. DIMETHYLAMINE.

1. Dimethylamine and camphoroxalic acid, in alcoholic solution, react to form *dimethylamine dimethylcamphoformolaminecarboxylate*,

which crystallizes from acetone in colorless needles, melting at 137°.5. Like the corresponding compound from diethylamine it is, apparently, formed by the direct combination of acid and base, without the loss of a molecule of water.

2. When the salt which has just been described is heated above the melting-point, it decomposes, similarly to the analogous diethyl compound and forms a substance of the same empirical formula as dimethylcamphoformeneamine, $C_{13}H_{21}NO$, but which, on account of the fact that it gives a color reaction with ferric chloride, does not seem to have that structure. It appears probable that its constitution is similar to that of the diethyl derivative and that its formula is,



It crystallizes from alcohol in colorless needles, melting at 63°.

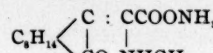
It is worthy of note that dimethylamine and diethylamine

are the only two secondary amines from which it has been possible to obtain derivatives with camphoroxalic acid. Methylaniline and ethylaniline entirely fail to give definite compounds under similar conditions; whether this is due to the general tendency of these two substances to yield oily salts, or to their feebler basic properties as compared with the aliphatic amines or to some other cause must, at present, remain uncertain.

### VIII. METHYLAMINE.

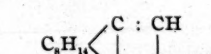
Methylamine forms two compounds with camphoroxalic acid:

1. *Methylamine methylcamphoformeneaminecarboxylate,*



which crystallizes from alcohol in slender, colorless needles, melting at 172°.

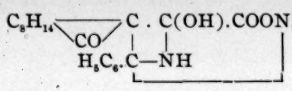
When this salt is heated above its melting-point, it forms *methylcamphoformeneamine,*



which crystallizes from ethyl acetate in colorless needles, melting at 131°.

### IX. BENZAMIDINE.

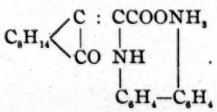
Camphoroxalic acid, in alcoholic solution, reacts with benzamidine, in equimolecular proportion, to form a colorless, crystalline compound, melting at 184°. At a slightly higher temperature it decomposes to a carbonaceous mass. Dilute acids and solutions of alkalies seem to have no effect upon the compound and ferric chloride, in alcoholic solution, does not give any color reaction. The substance has the empirical formula $C_{19}H_{24}O_4N_2$. Its constitution may, perhaps, be represented by the expression



but further work will be necessary to decide this point.

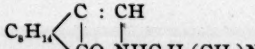
### X. BENZIDINE.

Benzidine reacts with camphoroxalic acid, in hot alcoholic solution, eliminating water and forming a greenish-yellow, crystalline mass, which melts at 190° and decomposes, when maintained at this temperature or heated for a short time at a higher one. The compound is, apparently, unchanged by the action of acids or alkalies and does not give any coloration with ferric chloride, in alcoholic solution. In view of these facts and of the properties of benzidine itself, it is probable that one of the amino groups has combined with the :COH group with the elimination of water, while the other has reacted with the carboxyl hydrogen to form a salt, as represented by the formula



### XI. 1,2,4-NITROTOLUIDINE.

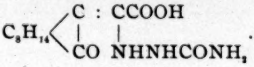
When nitrotoluidine ($CH_3 = 1$ ; $NH_2 = 2$ ; $NO_2 = 4$) is heated, at 150°, with camphoroxalic acid, in alcoholic solution, under pressure, for several hours, ***nitrotolylcamphoformeneamine,***



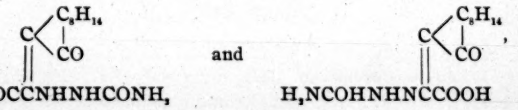
is obtained. It crystallizes readily from alcohol in minute, bright yellow needles, which melt at 192°. It was not possible to isolate the corresponding carboxylic acid or salt, although a number of experiments, under varying conditions, were made with this object.

### XII. SEMICARBAZINE.

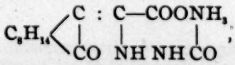
When semicarbazine and camphoroxalic acid react in the presence of acetic acid, a compound is formed with the composition of *semicarbazine camphoformeneaminecarboxylic acid*,



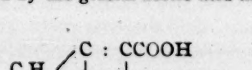
It crystallizes from alcohol in stout, colorless prisms, melting at 200°. When dissolved in boiling glacial acetic acid, crystals were deposited in the form of clusters of fine needles, which melt at 209°–210°. If the compound obtained from glacial acetic acid is dissolved in sodium carbonate and reprecipitated by acid, a gelatinous substance is formed which crystallizes from acetone in slender, colorless needles, melting at the same temperature as before, *viz.*, 209°–210°. These two substances have the same empirical formula and maintain their distinctive melting-points, even after heating for some time at 110°. They dissolve readily in sodium hydrogen carbonate and are reprecipitated by acids in the form of a jelly. With alcoholic ferric chloride, no color reaction is produced in either case. All these facts lead to one of two conclusions: either the compounds are stereoisomers of the maleic-fumaric type,



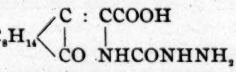
or there is the formation of an inner salt,



which is changed by the glacial acetic acid into the open-chain compound,



In the case of these semicarbazine derivatives we have represented the condensation as having taken place between the hydrazine nucleus and the camphoroxalic acid. Although this is in accordance with precedent, it may well be that in one or both compounds it is the carbamide group which has reacted, giving



and its stereoisomer. Further work will be necessary to decide between these various possibilities; the subject is being more fully investigated in this laboratory.

### XIII. ORTHOPHENYLENEDIAMINE.

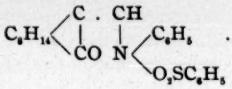
When orthophenylenediamine and camphoroxalic acid are allowed to react in alcoholic solution, at the ordinary temperature, there is formed the camphoquinoxaline compound, which was prepared by J. Bishop Tingle by the action of sodium camphoroxalate and also of ethyl camphoroxalate on orthophenylenediamine. It crystallizes from alcohol in bright yellow needles, which melt at 246°. The formation of this camphoquinoxaline, by the interaction of sodium camphoroxalate, ethyl camphoroxalate or camphoroxalic acid, respectively, is somewhat remarkable, as it shows the tendency of such a phenylene diamine derivative, in which the amino groups are in the ortho position, to form a five-membered ring compound, even under conditions where we should not expect such an action to take place.

PARAPHENYLENEDIAMINE was treated with camphoroxalic acid under the same conditions as were used for the ortho-compound and also under others, in the hope that it might react and throw some light on this question of ring formation, but no definite product could be obtained.

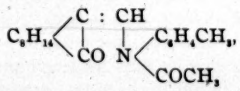
## ACTION OF ACYLATING AGENTS ON CAMPHOFORMENE DERIVATIVES.

The condensation compounds from primary amines, described in the preceding pages and those previously prepared

by Bishop Tingle, are represented as containing an imino group. This view of their constitution was based on the nature of the compounds formed from hydroxylamine and phenylhydrazine. It is very desirable to obtain some direct evidence on this point and, consequently, the study of acylating agents on camphoformene derivatives was commenced. Bishop Tingle had previously shown that, with phenylsulphonic chloride, by the Schotten-Baumann reaction, phenylcamphoformeneamine forms a compound which crystallizes from benzene in colorless needles and melts at 133°, but its composition was not determined. This work was repeated and a similar compound was obtained, it melted at 133° and, on standing in the air, soon began to decompose. It was found to be the *phenylcamphoformeneaminephenylsulphone*,



Acetyl chloride, when allowed to react with *p*-tolylcamphoformeneamine, replaces the iminic hydrogen and forms *acetyl p-tolylcamphoformeneamine*,



which is a colorless, crystalline compound, melting at 161°. The reaction of these two chlorides with the above typical camphoformeneamines, resulting in the elimination of hydrochloric acid and the formation of the sulphone and acetyl derivatives, seems to be rather conclusive evidence in favor of the structure which has been suggested for the camphoformeneamines and, as we know that these bodies are formed from the corresponding carboxylic acids by the elimination fo carbonic anhydride, the formulæ assigned to these acids also seem to be confirmed.

Chloracetyl chloride, when allowed to react with β-naphthylcamphoformeneamine, yields a colorless, crystalline compound, melting at 63°; unfortunately, on account of its instability, it could not be analyzed.

The following table (pp. 236–237) shows the various condensation compounds of camphoroxalic acid and amines which have hitherto been prepared. They are arranged in type classes and their melting-points are given. The compounds marked * have been previously described by J. Bishop Tingle and Alfred Tingle.[1] Those marked + contain the elements of 1 molecule of water more than is shown in the type formula. Their constitution has been discussed on p. 228 *et seq.* In cases where no definite compound could be isolated, the space in the table is occupied by a dash.

## EXPERIMENTAL.

Camphoroxalic acid was prepared according to the method worked out by J. Bishop Tingle[2] as follows:

Camphor (31.5 grams) and ethyl oxalate (22 grams) were dissolved in 400 cc. of anhydrous petroleum ether, of 85°–100° boiling-point and 3.5 grams of sodium wire were added. The mixture was boiled on a water-bath, with a reflux condenser, until the violent action had ceased and the sodium had almost entirely dissolved; it was then allowed to remain over night, at the ordinary temperature, protected from moisture. The solution, after standing, was well shaken with about an equal volume of ice-water and the petroleum ether extract separated from the water and dried over calcium chloride. The dried liquid was distilled, at first from the water-bath; when the temperature of the boiling liquid rises to almost 90°, the pressure is somewhat reduced and the distillation continued, care being taken not to allow the temperature of the liquid in the flask to rise above 130°; frequently it is unnecessary to heat above 120°–125°.

The aqueous solution was then well cooled and acidified with dilute sulphuric acid, then extracted three or four times with ether, until a portion of the fresh ether extract showed only a pale reddish-violet color with alcohol and ferric chloride. The ether was dried over calcium chloride and, after filtering, was distilled off and the residue added to that

[1] J. Am. Chem. Soc., 23, 364 (1901).
[2] *Ibid.*, 23, 364 (1901).

*Table I.*

| Amines. | $C_8H_{14}$ C : CCOONH$_3$R / CO NHR | $C_8H_{14}$ C : COOH / CO NHR | $C_8H_{14}$ C : CCH / CO NHR |
|---|---|---|---|
| I. $C_{10}H_7.NH_2$ $\beta$ | 169° | *m. p. 172°.5 | 173° |
| II. $C_6H_4.CH_3.NH_2$ [1 : 4] | 152° | 168° | 178° |
| III. $C_6H_5.CH_2.NH_2$ | 147°.5 | 140° | 96°.5 |
| IV. $C_{10}H_7.NH_2$ $\alpha$ | 165° | *170° | ——— |
| V. $CH_2C_6H_4NH_2$ [1 : 3] | 126° | 154° | ——— |
| VI. $NH(C_2H_5)_2$ | +139°.5 | ——— | 153° |
| VII. $NH(CH_3)_2$ | +137°.5 | ——— | 63° |
| VIII. $NH_2CH_2$ | 172° | ——— | 131° |
| IX. $C_6H_5C(NH_2) : NH$ | ——— | ——— | ——— |
| X. $NH_2C_6H_4.C_6H_4NH_2$ | ——— | ——— | ——— |
| XI. $CH_3^1C_6H_3^2NH_2.NO_2^4$ | ——— | ——— | 192° |
| XII. $NH_2CONHNH_2$ | 200° and 209°–210° | ——— | ——— |
| XIII. $C_6H_5NH_2$ | *158° | *174° | *166° |
| XIV. $NH_2OH$ | ——— | *+146°.5 | ——— |
| XV. $NH_3$ | ——— | *178° | ——— |
| XVI. $C_6H_4(NH_2)_2$ [1 : 2] | ——— | ——— | ——— |
| XVII. $NH_2NHC_6H_5$ | ——— | ——— | ——— |

$C_{10}H_{24}N_2O_4$ · 184°

$C_8H_{14}$ C : CCOONH$_3$ / CO NH — $C_6H_4C_6H_4$ 190°

$+C_{15}H_{20}N_2O_2$ 246°

$+C_8H_{14}$ C : CCOOC$_2$H$_5$ / CO NHNHC$_6$H$_5$ 212°

*Table I. (Continued).*

| Amines. | $C_8H_{14}$ C : CCOONH$_3$R / CO NHR | $C_8H_{14}$ C : CCOOH / CO NHR | $C_8H_{14}$ C : CH / CO NHR |
|---|---|---|---|
| XVIII. $CH_2CONHNHC_6H_5$ | —— | —— | —— |
| XIX. $OC(NH_2)_2$ | —— | —— | —— |
| XX. $NH_2C_6H_4NO_2$ [1 : 4] | —— | —— | —— |
| XXI. $CH_3COC_6H_4NH_2$ [1 : 4] | —— | —— | —— |
| XXII. $C_6H_5NHCH_3$ | —— | —— | —— |
| XXIII. $C_6H_5NHC_2H_5$ | —— | —— | —— |
| XXIV. $C_6H_5NHCH_2C_6H_5$ | —— | —— | —— |
| XXV. $C_2H_4(NH_2)_2$ | —— | —— | —— |
| XXVI. $C_6H_5NHNHCH_2C_6H_5$ | —— | —— | —— |
| XXVII. $(NH_2)_2C : NH$ | —— | —— | —— |
| XXVIII. $CH<\begin{matrix}CH.CH\\ \\ CH.CH\end{matrix}>N$ | —— | —— | —— |
| XXIX. $C_6H_5N(CH_2)_2$ | —— | —— | —— |
| XXX. $CH_3C_6H_4NH_2$ [1 : 2] | —— | —— | —— |
| XXXI. $NH_2NHC_6H_4Br$ [1 : 4] | —— | —— | —— |
| XXXII. $NH_2NH_2$ | —— | —— | —— |

from the petroleum ether extract. This residue was extracted, several times, by boiling with a 10 per cent solution of potassium hydroxide, until the filtrate, after acidification, no longer gave a marked color with alcohol and ferric chloride. The alkaline solution, from the filtered extracts, was then acidified with dilute sulphuric acid and, after standing several hours, the crystalline precipitate was filtered off. This crystalline mass was purified by recrystallization from petroleum ether, by means of a Soxhlet apparatus. The mother-liquors from the recrystallizations and the residue in the Soxhlet apparatus were treated with sodium carbonate, the solution filtered, acidified and the resulting precipitate recrystallized.

## CAMPHOROXALIC ACID DERIVATIVES.

### METALLIC SALTS OF CAMPHOROXALIC ACID.

*Copper Camphoroxalate.*—The acid (1 molecule) and copper nitrate (0.5 molecule) were separately dissolved in 50 per cent alcohol, the solutions mixed and allowed to evaporate at the ordinary temperature. Although the pure and dry copper salt does not melt below 275°, it was found that, if the solution was heated on a water-bath, to remove the excess of alcohol, the green salt formed, with part of the solvent, an oily layer which was extremely difficult to purify. When it is allowed to crystallize at the ordinary temperature, it is deposited as a fine, green, crystalline powder, which melts and decomposes at 275°. With ferric chloride, in alcoholic solution, this salt gives no coloration. If an alcoholic solution of the salt is heated for some time at 100°, it undergoes decomposition and deposits cuprous oxide. Analysis:

2.1686 grams salt gave 0.0474 gram CuO.

| | Calculated for $C_8H_{14}\begin{cases} C : COCOO \\ CO \quad\quad Cu \end{cases}$. | Found. |
|---|---|---|
| Cu | 22.28 | 22.46 |

The proportion of the reacting substances was varied, in the hope that another salt, of different composition, might be

formed, but, in all cases, the resulting compound was identical with the one described above.

*2. Silver Camphoroxalate.*—Silver nitrate and camphoroxalic acid were allowed to react in a solution of 50 per cent alcohol and, on allowing the solvent to evaporate spontaneously, a colorless, crystalline mass was obtained, which was purified by repeated recrystallization from alcohol. The resulting compound was found to melt and decompose at 137°. Analysis:

0.2975 gram salt gave 0.0965 gram Ag.

| | Calculated for $C_8H_{14}\langle^{C:COHCOOAg}_{CO}$. | Found. |
|---|---|---|
| Ag | 32.63 | 32.47 |

As in the preparation of the copper salt, different proportions of silver nitrate and camphoroxalic acid were allowed to react but, in this case also, only one compound could be isolated.

*3. Barium Camphoroxalate.*—Barium nitrate (1 molecule) and camphoroxalic acid (2 molecules), in a solution of 50 per cent alcohol, were allowed to evaporate. These deposited a colorless, crystalline compound, which was recrystallized from alcohol. With ferric chloride and alcohol a reddish-violet color, characteristic of the presence of the enol grouping, was produced. Analysis:

0.1728 gram salt gave 0.0682 gram $BaSO_4$.

| | Calculated for $\left(C_8H_{14}\langle^{C:COHCOO}_{CO}\right)_2Ba$. | Found. |
|---|---|---|
| Ba | 23.56 | 23.21 |

The proportions of the reacting substances were varied, as in the preceding cases, but no other salt could be obtained.

*4. Calcium Camphoroxalate.*—Calcium nitrate (1 molecule) and camphoroxalic acid (2 molecules) were mixed in solution of 50 per cent alcohol, under the same conditions as in the case of the barium salt; on evaporation and recrystallization from alcohol, colorless crystals were deposited. Analysis:

0.2067 gram salt gave 0.0537 gram $CaSO_4$.

| | Calculated for $\left(C_8H_{14}\begin{cases}C : COHCOO\\ \vert\\ CO\end{cases}\right)_2Ca$. | Found. |
|---|---|---|
| Ca | 8.22 | 8.4 |

In the case of the calcium salt also, only one compound could be obtained.

5. *Ferric Camphoroxalate.*—Ferric chloride (1 molecule) and camphoroxalic acid (2 molecules) were mixed in solution of 50 per cent alcohol. A deep, reddish-violet coloration was produced but from no solvent could a crystalline compound be obtained and the viscous substance, deposited by the evaporation of the original liquid to dryness, gave percentages of iron which showed that it had no definite composition, hence the following method was employed: The alcoholic solution of the reaction-product, formed by the camphoroxalic acid and ferric chloride, was diluted with water in order to precipitate any unchanged camphoroxalic acid and, at the same time, to dissolve the dark-red substance in solution in the alcohol. After filtering, ether was added to the liquid, but, on account of the presence of free hydrochloric acid which had been formed by the reaction of the camphoroxalic acid and ferric chloride, the ether dissolved and formed a homogenous solution with the original liquid. When this mixed ethereal-aqueous liquid was saturated with sodium chloride the ether took up the red compound and separated from the aqueous layer; this latter was removed and the ethereal solution dried over calcium chloride. The ether was then evaporated from the water-bath. A glassy, almost black mass remained. It is soluble, to a slight extent, in boiling sodium carbonate solution. The compound should, probably, be regarded as being camphoroxalic acid in which the hydrogen atom of the enol group :COH has been replaced by iron, while the carboxyl group remained intact on account of the presence of hydrochloric acid in the liquid during the reaction. Analysis:

0.2095 gram substance gave 0.0235 gram $Fe_2O_3$.

| | Calculated for $\left(C_8H_{14}\begin{cases}C : COCOOH\\ \vert\\ CO\end{cases}\right)_3Fe$. | Found. |
|---|---|---|
| Fe | 7.72 | 7.8 |

## AMINE DERIVATIVES OF CAMPHOROXALIC ACID.

### I. β-NAPHTHYLAMINE.

1. β-Naphthylamine (6.4 grams = 2 molecules) and camphoroxalic acid (5 grams = 1 molecule) were mixed in boiling alcoholic solution, which was then kept at about 100°, on a water-bath, for a few minutes. Fine, yellow needles soon began to separate out and, on cooling, a mass of such crystals was deposited. The yield was almost quantitative. The compound is fairly readily soluble in hot alcohol and is purified by recrystallization from it. The purified compound was deposited in the form of fine needles, of a pale yellow color and melted at 169°, with the evolution of a gas. Analysis showed it to be *β-naphthylamine β-naphthylcamphoformeneaminecarboxylate.*

0.1723 gram substance gave 8.6 cc. N at 18° and 770 mm.

| | Calculated for $C_8H_{14}\begin{cases} C : CCOONH_3C_{10}H_7 \\ CO\ NHC_{10}H_7 \end{cases}$ | Found. |
|---|---|---|
| N | 5.66 | 5.74 |

This salt when treated, in alcoholic solution, with ferric chloride, did not give the violet-red color characteristic of the enol grouping.

2. When the above compound is heated with a solution of sodium hydroxide, it dissolves, forming sodium β-naphthylcamphoformeneaminecarboxylate and liberating β-naphthylamine, which is deposited, on cooling the liquid and was identified by its melting-point, 112°. On acidification of the solution of the sodium salt with dilute hydrochloric acid, the free β-naphthylcamphoformeneaminecarboxylic acid is precipitated. It was purified by recrystallization from benzene and is deposited in yellow needles, melting at 172°.5–173°. This corresponds to the melting-point obtained for the same compound which was prepared by J. Bishop Tingle.[1] The acid dissolves readily in sodium carbonate solution with the evolution of carbonic anhydride and, in alcoholic solution, produces no red color with ferric chloride.

3. When β-naphthylamine β-naphthylcamphoformeneamine-

[1] J. Am. Chem. Soc., **23**, 375 (1901).

carboxylate is heated above its melting-point, it gives off a gas which was proved to be carbonic anhydride by the production of barium carbonate, when it was led into a solution of barium hydroxide. A white solid sublimes into the upper part of the tube in which the fusion is being made and, by its melting-point, was shown to be β-naphthylamine. The fused material, after the evolution of gas had ceased, is purified by means of alcohol and crystallizes in pale yellow needles, melting at 173°. Analysis showed it to be ***β-naphthylcamphoformeneamine.***

0.1783 gram substance gave 7.1 cc. N at 12° and 760 mm.

| | Calculated for $C_8H_{14}\begin{cases} C:CH \\ \vert \\ CO\ NHC_{10}H_7 \end{cases}$ | Found. |
|---|---|---|
| N | 4.59 | 4.73 |

With ferric chloride, in alcoholic solution, no violet-red color was produced. When β-naphthylcamphoformeneaminecarboxylic acid is heated above its melting-point it gives off carbonic anhydride and forms a compound, melting at 173°, identical with that formed from the β-naphthylamine β-naphthylcamphoformeneaminecarboxylate by heating.

### II. PARATOLUIDINE.

Camphoroxalic acid (5 grams = 1 molecule) and paratoluidine (4.8 grams = 2 molecules) were mixed in boiling alcoholic solution, which, on cooling, deposited a mass of fine yellow needles. The yield seemed to be nearly quantitative. The compound is soluble in alcohol and is purified by recrystallization from it. The purified compound crystallizes in slender, yellow needles and melts at 152°, with the evolution of a gas. With ferric chloride, in alcoholic solution, it gave no color reaction. Analysis proved it to be ***paratoluidine paratolylcamphoformeneaminecarboxylate.***

0.1818 gram substance gave 10.2 cc. N at 13° and 765 mm.

| | Calculated for $C_8H_{14}\begin{cases} C:CCOONH_2C_6H_4CH_3 \\ \vert \\ CO\ NHC_6H_4CH_3 \end{cases}$ | Found. |
|---|---|---|
| N | 6.66 | 6.67 |

2. When the above compound is heated with sodium hy-

droxide solution, it dissolves, forming *sodium paratolylcamphoformeneaminecarboxylate* which, on acidification with dilute hydrochloric acid, precipitates the free *paratolylcamphoformeneaminecarboxylic acid;* this is insoluble in water and forms a pale yellow mass. The substance, after recrystallization from benzene, is deposited in yellow needles and melts at 168°, with the evolution of a gas. It dissolves in sodium carbonate solution with the liberation of carbonic anhydride and, with an alcoholic solution of ferric chloride, produces no color. Analysis showed it to be *paratolylcamphoformeneaminecarboxylic acid.*

0.1605 gram substance gave 6.2 cc. N at 6° and 770 mm.

| | Calculated for $C_8H_{14}\langle \overset{C : CCOOH}{\underset{CO\ NHC_6H_4CH_3}{|}}$ | Found. |
|---|---|---|
| N | 4.47 | 4.64 |

3. When the paratoluidine paratolylcamphoformeneaminecarboxylate is heated above its melting-point it gives off a gas which was proved to be carbonic anhydride by the production of barium carbonate, when it was led into a solution of barium hydroxide. When the tube in which the fusion is being made is allowed to cool, a white, crystalline solid appears in its upper part; this, by its melting-point, 42°.5, was demonstrated to be paratoluidine. The fused material, after the evolution of gas had ceased, was recrystallized from alcohol and is deposited in very pale yellow crystals, melting at 178°. With alcoholic ferric chloride no color is produced. Analysis showed it to be *paratolylcamphoformeneamine.*

0.1710 gram substance gave 7.8 cc. N at 12° and 755 mm.

| | Calculated for $C_8H_{14}\langle \overset{C : CH}{\underset{CO\ NHC_6H_4CH_3}{|}}$ | Found. |
|---|---|---|
| N | 5.20 | 5.37 |

When paratolylcamphoformeneaminecarboxylic acid is heated above its melting-point it gives off carbonic anhydride and forms a compound, melting at 178°, identical with the one just described, which is formed by heating the paratoluidine salt of this acid.

III. BENZYLAMINE.

1. Camphoroxalic acid (5 grams = 1 molecule) and benzylamine (4.6 grams = 2 molecules) were mixed in hot alcoholic solution and, after evaporating off part of the solvent on the water-bath and cooling, a colorless, crystalline mass was gradually deposited. After recrystallization from alcohol it was obtained in the form of distorted rhombohedra, melting at 147°.5 with the evolution of a gas. With alcoholic ferric chloride no color was produced. Analysis showed it to be *benzylamine benzylcamphoformeneaminecarboxylate.*

0.2251 gram substance gave 15.7 cc. N at 18° and 770 mm.

| | Calculated for $C_8H_{14}\begin{cases} C : CCOONH_3CH_2C_6H_5 \\ \vert \quad \vert \\ CO \quad NHCH_2C_6H_5 \end{cases}$ | Found. |
|---|---|---|
| N | 7.95 | 8.16 |

2. When the above compound is heated with sodium hydroxide solution it dissolves, forming sodium benzylcamphoformeneaminecarboxylate. The addition of dilute hydrochloric acid, in excess, to this solution produces a gummy precipitate, which solidifies after standing in contact with water and, on recrystallization from ethyl acetate, forms colorless crystals, melting at 140°. In sodium carbonate solution it dissolves with the evolution of carbonic anhydride and, with alcoholic ferric chloride, produces no color. Analysis proves it to be *benzylcamphoformeneaminecarboxylic acid.*

0.2035 gram substance gave 0.5396 gram $CO_2$ and 0.1395 gram $H_2O$.

| | Calculated for $C_8H_{14}\begin{cases} C : CCOOH \\ \vert \quad \vert \\ CO \quad NHCH_2C_6H_5 \end{cases}$ | Found. |
|---|---|---|
| C | 72.52 | 72.35 |
| H | 7.35 | 7.6 |

3. Heated above its melting-point, benzylamine benzylcamphoformeneaminecarboxylate gives off a gas which proved to be carbonic anhydride by the production of barium carbonate, when it was passed into a solution of barium hydroxide. The fused material, after the evolution of gas had

ceased, was recrystallized from ethyl acetate and is deposited in colorless prisms, melting at 96°.5. With alcoholic ferric chloride no color is produced. Analysis showed it to be *benzylcamphoformeneamine.*

0.1885 gram substance gave 9.8 cc. N at 16° and 762 mm.

| | Calculated for $C_8H_{14}\langle \overset{C:CH}{\underset{CO\ NHCH_2C_6H_5}{|\ \ |}} \rangle$ | Found. |
|---|---|---|
| N | 6.07 | 5.45 |

If benzylcamphoformeneaminecarboxylic acid is heated above its melting-point it also gives off carbonic anhydride and forms a compound, melting at 96°.5, identical with that formed by heating the benzylamine salt of the acid.

### IV. α-NAPHTHYLAMINE.

Camphoroxalic acid (5 grams = 1 molecule) and α-naphthylamine (6.4 grams = 2 molecules) were mixed in alcoholic solution. On evaporating the solvent, greenish-yellow crystals were found which, after purification from alcohol, melt at 165°, with the evolution of gas. With ferric chloride, in alcoholic solution, no color is produced. Analysis proved it to be *α-naphthylamine α-naphthylcamphoformeneaminecarboxylate.*

0.1532 gram substance gave 7.5 cc. N at 16° and 766 mm.

| | Calculated for $C_8H_{14}\langle \overset{C:CCOONH_3C_{10}H_7}{\underset{CO\ NHC_{10}H_7}{|\ \ |}} \rangle$ | Found. |
|---|---|---|
| N | 5.66 | 5.75 |

The above salt dissolves when treated with sodium hydroxide solution, forming *sodium α-naphthylcamphoformeneaminecarboxylate,* which, on acidification with dilute hydrochloric acid, forms a yellow precipitate; this, after crystallization from benzene, melts at 170° and is found to be identical with the same compound prepared in another way by Bishop Tingle. It dissolves in sodium carbonate with the evolution of carbonic anhydride and, with alcoholic ferric chloride, produces no color.

3. When either of the above α-naphthylamine compounds

was heated, in order to obtain a camphoformeneamine derivative, a gummy substance was obtained, which could not be induced to crystallize from any solvent.

### V. METATOLUIDINE.

1. Camphoroxalic acid (5 grams = 1 molecule) and metatoluidine (4.8 grams = 2 molecules) were allowed to react in alcoholic solution; after evaporation there were deposited fine needles of a pale lemon color which, when recrystallized from alcohol, melted at 126°. With alcoholic ferric chloride no color was produced. Analysis showed this substance to be *metatoluidine metatolylcamphoformeneaminecarboxylate.*

0.3153 gram substance gave 19 cc. N at 25° and 765 mm.

| | Calculated for $C_8H_{14}\langle \begin{matrix} C : CCOONH_2C_6H_4CH_3 \\ \vert \\ CO\ NHC_6H_4CH_3 \end{matrix}$ | Found. |
|---|---|---|
| N | 6.66 | 6.78 |

2. The above salt, when treated with a solution of sodium hydroxide, dissolves, forming *sodium metatolylcamphoformeneaminecarboxylate*, which, on acidification with dilute hydrochloric acid, gives a yellow precipitate. After purification from benzene, crystals are deposited melting at 154°. They dissolve in sodium carbonate solution with the evolution of carbonic anhydride and, with alcoholic ferric chloride, give no color. Analysis shows it to be *metatolylcamphoformeneaminecarboxylic acid.*

0.1497 gram substance gave 5.65 cc. N at 10° and 770 mm.

| | Calculated for $C_8H_{14}\langle \begin{matrix} C : CCOOH \\ \vert \\ CO\ NHC_6H_4CH_3 \end{matrix}$ | Found. |
|---|---|---|
| N | 4.47 | 4.58 |

3. Both metatolylcamphoformeneaminecarboxylic acid and its metatoluidine salt, on heating, gave a gum, which could not be obtained pure enough for analysis.

### VI. DIETHYLAMINE.

1. Camphoroxalic acid (5 grams = 1 molecule) was allowed to react with an alcoholic solution (3.4 grams = 2 molecules)

of diethylamine ; a compound crystallizing in colorless needles was obtained which, when purified by recrystallization from alcohol, melts at 139°.5 with the evolution of a gas. With alcoholic ferric chloride it gives no color reaction. By analysis the compound is shown to be *diethylamine diethylcamphoformolaminecarboxylate.*

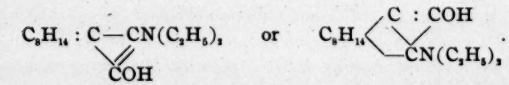
0.1983 gram substance gives 13.4 cc. N at 21° and 769 mm.

| | Calculated for $C_8H_{14}\langle^{CH.COHCOONH_2(C_2H_5)_2}_{CO\ N(C_2H_5)_2}$ | Found. |
|---|---|---|
| N | 7.55 | 7.80 |

The diethylamine solution used in the preparation of this compound was prepared by dissolving diethylamine hydrochloride in absolute alcohol, adding the required amount of potassium hydroxide and filtering off the insoluble potassium chloride.

2. When treated with sodium hydroxide solution the carboxylate just described dissolves but, on acidification with dilute hydrochloric acid, it is decomposed into camphoroxalic acid and diethylamine. No method of treatment could be devised by which free diethylcamphoformolaminecarboxylic acid could be obtained.

3. When diethylamine diethylcamphoformolaminecarboxylate is heated above its melting-point, diethylamine, water and carbonic anhydride are given off and, after purification of the fused material, by crystallization from acetone, the product melts at 153°. With alcoholic ferric chloride the reddish-violet color is produced, which is so characteristic of the enol grouping. By analysis it is found to have an empirical formula identical with that of diethylcamphoformeneamine, but, on account of its behavior towards ferric chloride, its constitution seems, as previously explained (p. 228), to be represented by the formula



Analysis :

0.2045 gram substance gave 8.1 cc. N at 16° and 762 mm.

| | Calculated for $C_{18}H_{29}ON$. | Found. |
|---|---|---|
| N | 4.56 | 4.68 |

VII. DIMETHYLAMINE.

1. Camphoroxalic acid (5 grams = 1 molecule) and dimethylamine (2 grams = 2 molecules) were allowed to react in alcoholic solution and, after part of the solvent had evaporated spontaneously, a crystalline compound was obtained. After recrystallization from acetone, colorless needles were deposited, melting at 137°.5 with the evolution of a gas. With alcoholic ferric chloride it produced no color reaction. Analysis showed it to be *dimethylamine dimethylcamphoformolaminecarboxylate.* Analysis :

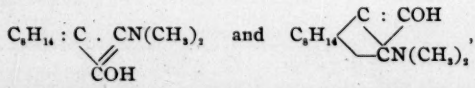
I. 0.2000 gram substance gave 0.4452 gram $CO_2$ and 0.1661 gram $H_2O$.

II. 0.2135 gram substance gave 0.4818 gram $CO_2$ and 0.1770 gram $H_2O$.

| | Calculated for $C_8H_{14}\begin{cases}\text{CH.COHCOONH}_2(CH_3)_2\\ \text{CO N}(CH_3)_2\end{cases}$ | Found. I. | II. |
|---|---|---|---|
| C | 61.14 | 60.71 | 61.58 |
| H | 9.55 | 9.29 | 9.27 |

2. When dimethylamine dimethylcamphoformolaminecarboxylate is treated with sodium hydroxide solution it dissolves but, on acidification with dilute hydrochloric acid, decomposes into camphoroxalic acid and dimethylamine.

3. When heated to 140°, dimethylamine dimethylcamphoformolaminecarboxylate gives off water, carbonic anhydride and dimethylamine and forms a compound which, when purified by recrystallization from acetone, melts at 63°. With alcoholic ferric chloride it gives a purple color. The alternative formulæ,



for this compound are discussed on p. 228. Analysis :

0.2458 gram substance gave 14.8 cc. N at 19° and 770 mm.

| | Calculated for $C_{18}H_{31}ON$. | Found. |
|---|---|---|
| N | 6.77 | 7.01 |

VIII. METHYLAMINE.

1. Camphoroxalic acid (5 grams = 1 molecule) and methylamine (2.8 grams = 2 molecules) were mixed in alcoholic solution. After evaporation of part of the solvent, colorless needles were deposited; they were purified by recrystallization from alcohol and melted at 172°. With alcoholic ferric chloride no color reaction was produced. Analysis proved the compound to be *methylamine methylcamphoformeneaminecarboxylate.* Analysis:

0.2147 gram substance gave 20 cc. N at 14° and 766 mm.

| | Calculated for $C_8H_{14}\begin{cases} C : CCOONH_3CH_3 \\ \vert \quad\quad \vert \\ CO\ NHCH_3 \end{cases}$. | Found. |
|---|---|---|
| N | 10.51 | 11.04 |

2. When treated with sodium hydroxide, the above salt dissolves but, on acidification with dilute hydrochloric acid, decomposes into camphoroxalic acid and methylamine.

3. Upon heating at 175°, methylamine methylcamphoformeneaminecarboxylate gives off methylamine and carbonic anhydride and forms a compound which, when recrystallized from ethyl acetate, melts at 131°. With alcoholic ferric chloride no color reaction is produced. Analysis proved it to be *methylcamphoformeneamine.* Analysis:

0.2131 gram substance gave 13.3 cc. N at 11° and 766 mm.

| | Calculated for $C_8H_{14}\begin{cases} C : CH \\ \vert \quad \vert \\ CO\ NHCH_3 \end{cases}$. | Found. |
|---|---|---|
| N | 7.25 | 7.50 |

IX. BENZAMIDINE.

Free benzamidine (2.2 grams = 1 molecule) was obtained by dissolving the hydrochloride in absolute alcohol, adding the required amount of potassium hydroxide and filtering off the insoluble potassium chloride. When camphoroxalic acid (5

grams = 1 molecule) is allowed to react with such an alcoholic solution of benzamidine and the solvent is permitted to evaporate spontaneously, a compound is obtained which may be purified by recrystallization from alcohol. It is deposited in colorless prisms; these melt at 184°, evolve a gas, char and decompose. With alcoholic ferric chloride no color reaction is produced and neither acid nor alkali seem to cause any change in the composition of the compound. When heated above its melting-point, it decomposes completely to a carbonaceous mass, from which it is impossible to obtain any definite compound. It did not dissolve in sodium carbonate solution. Analysis proved it to have the empirical formula $C_{19}H_{24}O_4N_2$. Its probable constitution is discussed on p. 231.

0.1539 gram substance gave 0.3723 gram $CO_2$ and 0.0963 gram $H_2O$.

0.2147 gram substance gave 15.5 cc. N at 19° and 766 mm.

| | Calculated for $C_{19}H_{24}N_2O_4$. | Found. |
|---|---|---|
| C | 66.27 | 65.93 |
| H | 6.97 | 7.002 |
| N | 8.14 | 8.30 |

X. BENZIDINE.

Camphoroxalic acid (5 grams = 1 molecule) and benzidine (4 grams = 1 molecule) were mixed in hot alcoholic solution. When cooled, this deposited a dense mass of greenish-yellow, microscopic needles, which, on account of its very sparing solubility in all the ordinary organic media, was extracted with ether, to remove any camphoroxalic acid and benzidine. The residue, after this treatment, formed a fine powder, which gave no color reaction with alcoholic ferric chloride and was not affected by acids or alkalies. It melts at 190° and, when heated above this temperature, it decomposed to a carbonaceous mass. It is insoluble in sodium carbonate. Analysis proved it to have the empirical formula $C_{24}H_{26}O_2N_2$; its possible constitution is discussed on p. 231.

0.1489 gram substance gave 9.4 cc. N at 21° and 775 mm.

| | Calculated for $C_{24}H_{26}O_2N_2$. | Found. |
|---|---|---|
| N | 7.18 | 7.31 |

XI. PARANITROORTHOTOLUIDINE.

When camphoroxalic acid (5 grams = 1 molecule) and nitrotoluidine (6.8 grams = 2 molecules) are heated at 150°, under pressure, in alcoholic solution, for 4 hours, a yellow compound is obtained which is purified by recrystallization from alcohol. It is deposited in bright yellow needles, melting at 192°. This compound is unaffected by acids or alkalies, does not dissolve in sodium carbonate and produces no color reaction with ferric chloride, in alcoholic solution. Considerable difficulty was experienced in the combustion of the substance for the determination of nitrogen; even when the heating was done most cautiously, explosions occurred, so that the analytical results were unreliable. These explosions were probably due to the presence of the nitro group in the compound. The difficulty was overcome, in a thoroughly satisfactory manner, by mixing the substance with aluminium powder; under these conditions the nitrogen was evolved during the combustion in a stream which could be easily regulated. Analysis:

0.2145 gram substance gave 8.8 cc. N at 17° and 765 mm.

| | Calculated for $C_8H_{14}\begin{cases} C:CH \\ CO\ NHC_6H_3(CH_3)NO_2 \end{cases}$ | Found. |
|---|---|---|
| N | 4.66 | 4.79 |

XII. SEMICARBAZINE.

Semicarbazine hydrochloride (5 grams = 2 molecules) was dissolved in as little cold water as possible and added to an alcoholic solution of potassium acetate (5 grams = 2 molecules); this solution was then mixed with an alcoholic solution of camphoroxalic acid (5 grams = 1 molecule). After evaporation of most of the alcohol on the water-bath the solution was greatly diluted with water; a white, crystalline precipitate was produced which, on purification by recrystallization from alcohol, formed colorless prisms, melting at 200°. When dissolved in boiling glacial acetic acid and precipitated by the addition of alcohol, clusters of colorless, microscopic needles are deposited; these melt at 209°–210° and correspond to the

compound described by Bishop Tingle,[1] as one of two substances formed by the action of semicarbazine on potassium camphoroxalate, in alcoholic solution, at 100°, under pressure. The presence of a second compound, stated by him to be deposited from acetone in colorless needles, melting at 218°, was not observed ; it is, apparently, not formed under the conditions employed by us. When the compound melting at 209°–210°, obtained from acetic acid solution, was dissolved in sodium carbonate solution and precipitated by acids it formed a jelly which, after having been dried and recrystallized from acetic acid, had the same melting-point as before, *viz.*, 209°–210°. If the original compound from alcohol, melting at 200°, is recrystallized from acetone, its melting-point remains constant. With alcoholic ferric chloride neither substance produces a color reaction. Both dissolve readily in sodium carbonate and, as has been stated, are precipitated by acids from this solution as colorless jellies. Analysis showed that both compounds have the composition of *semicarbazinecamphoformeneaminecarboxylic acid*.

0.2145 gram substance gave 0.4373 gram $CO_2$ and 0.1261 gram $H_2O$.

| | Calculated for $C_8H_{14}\langle \overset{C : CCOOH}{\underset{CO\ NHNHCONH_2}{\vert\ \vert}} \rangle$ | Found. |
|---|---|---|
| C | 55.6 | 55.5 |
| H | 6.76 | 6.57 |

The possible constitution and relationship of these compounds has been discussed on p. 232.

### XII. ORTHOPHENYLENEDIAMINE.

Camphoroxalic acid (5 grams = 1 molecule) and orthophenylenediamine (2.4 grams = 1 molecule) were allowed to react in alcoholic solution. The evaporation of the solvent yielded a deposit of fine yellow needles, which melt at 246°. This substance is identical with the compound obtained by J. Bishop Tingle.[2] The proportional quantities of the reacting

[1] J. Am. Chem. Soc., **23**, 373 (1901).
[2] *Ibid.*, **23**, 375 (1901).

materials and the conditions of the experiment were varied, but, in all cases, the same compound was obtained.

The action of camphoroxalic acid on acetylphenylhydrazine, carbamide, paranitraniline, paramineacetophenone, methylaniline, ethylaniline, benzylaniline, ethylenediamine, benzylphenylhydrazine, quinoline, pyridine, dimethylaniline, orthotoluidine, parabromphenylhydrazine and hydrazine was tried, under conditions similar to those already described for other amines, but in no case could a definite compound be obtained. The reaction-products were usually gummy substances which could not be obtained in a crystalline form. They were heated for some time at 150°–180°, in the hope of forming compounds of the camphoformeneamine type, but from these products also no crystalline derivatives could be isolated by the use of the ordinary organic solvents.

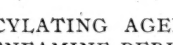
Possibly further investigation of the compounds may result in their purification by distillation, under very low pressures.

## ACTION OF ACYLATING AGENTS ON CAMPHOFORMENEAMINE DERIVATIVES.

Paratolylcamphoformeneamine (3 grams = 1 molecule) and acetyl chloride (2.6 grams = 3 molecules) were boiled in solution of anhydrous ether, for about 6 hours; the ether was then evaporated, leaving a compound which crystallized from alcohol in colorless needles, melting at 161°. Analysis showed it to be *acetyl paratolylcamphoformeneamine.*

0.1056 gram substance gave 0.2992 gram $CO_2$ and 0.0705 gram $H_2O$.

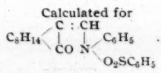
0.5403 gram substance gave 0.0983 gram $Mg_2P_2O_7 = 0.0747$ gram $C_2H_3O$.

| | Calculated for  | Found. |
|---|---|---|
| C | 77.4 | 77.26 |
| H | 7.74 | 7.47 |
| $CH_3CO$ | 13.78 | 13.82 |

Phenylcamphoformeneamine was treated with phenylsul-

phonic chloride, by the Schotten-Baumann method; (1 gram = 1 molecule) of phenylcamphoformeneamine was shaken with (1 gram = 7 molecules) of sodium hydroxide, in 10 per cent aqueous solution and (3.5 grams = 5 molecules) of phenylsulphonic chloride, which were added alternately and in small quantities; a compound is finally obtained which, by crystallization from benzene, is deposited in stout, colorless needles, melting at 133°. Analysis shows it to be *phenylcamphoformeneaminephenylsulphone.*

0.2246 gram substance gave 0.1311 gram $BaSO_4$.

| | Calculated for  | Found. |
|---|---|---|
| S | 8.10 | 8.07 |

$\beta$-Naphthylcamphoformeneamine (2 grams = 1 molecule) and chloracetyl chloride (2.1 grams = 3 molecules), when boiled for some hours, in anhydrous ether, react to form a bright red substance, which was purified by distillation under diminished pressure. It boiled at 116°, under 45 mm. pressure and condensed to a colorless, crystalline solid, which could be further purified by means of petroleum ether. From this it was deposited in colorless needles, melting at 63°. The compound dissolved in sodium hydrogen carbonate, with evolution of carbonic anhydride and gave no color reaction with ferric chloride. It is very unstable and consequently could not be obtained in a state of purity sufficient to give concordant results on analysis.

The work described in the preceding pages will be continued and extended in various directions. The cost of the greater part of the chemicals which we have used in carrying it out has been defrayed by a grant from the Carnegie Institution; for this we desire to express our thanks and obligations.

JOHNS HOPKINS UNIVERSITY,
April, 1905.

CONVERSATIONS ON CHEMISTRY. FIRST STEPS IN CHEMISTRY. By W. OSTWALD, Professor of Chemistry in the University of Leipzig. Authorized translation by ELIZABETH CATHERINE RAMSAY. Part I. General Chemistry. First edition. New York: John Wiley & Sons; London: Chapman & Hall. 1905. pp. 250. Price, $1.50.

It is difficult to form an opinion of the merits of this book. In some respects it is very good, in others very disappointing. Let us quote at length from the preface:

"By a stroke of good fortune the 'Schule der Chemie' of Stöckhardt, whose memory still lingers among us, was the first text-book of chemistry placed in my hands and it influenced the whole of my subsequent activity in science. Owing to the carefully thought-out directness in presenting the facts to the pupil, the skill in selecting experiments suitable to the physical and mental powers of the beginner, I have never lost touch with experiments, although I have been chiefly occupied with general questions of science. The request of the publishers who used to issue this work that I should write a modern Stöckhardt was both an honor and an opportunity of paying off an old debt of thankfulness."

Ostwald then gives his reasons for thinking that the first lessons in chemistry should be in general chemistry, as underlying inorganic and organic chemistry. He closes the preface by alluding to the dialogue form as seeming "most suitable—while the impression it makes is much more penetrating and lively."

Of the value of Stöckhardt's book the reviewer has no doubt, for a study of it, with laboratory experiments, was of the greatest service to him, as a beginner, in a place where the regular laboratory course was merely analytical. A modern revision of Stöckhardt, appealing, as the original did, to serious students of chemistry, would be a welcome publication.

One may also agree with Ostwald that the first part of such a book should be "general" chemistry.

Ostwald's treatment of the subject—barring the dialogue—is always clear and ingenious and generally shows the master hand. Yet it seems to the reviewer that *the use made in this work* of the dialogue form, renders the book valueless to those who would have profited by Stöckhardt, as it can only appeal to young boys, if indeed it would appeal to them.

Such an opinion of a book by Ostwald requires explanation. Quotations from any page will show that it would not suit a high school boy. Here is a specimen from the chapter on hydrogen:

"Master—You know that iron combines easily with oxygen?

Pupil—Yes, it burns with a lovely rain of sparks.

Master—Now the iron acts on the steam in such a way that it takes the oxygen and combines to form iron oxide; the hydrogen then remains over. Iron oxide is a solid substance even at a red heat and, therefore, remains where the iron was; but hydrogen is a gas and passes further along; it can then be collected over water in the same way as oxygen.

Pupil—That seems very strange to me.

Master—I will give you a simile. Oxygen is a bone which the cat hydrogen had to start with. Then the dog iron comes along and takes the bone from the cat, and the cat hydrogen must run away without the bone."

This is kindergarten talk, but no child and no normal boy under 16 could comprehend the teaching of this book, no matter how colloquial the style.

Here is another specimen, from the same chapter, which illustrates difficulties for reviewer and translator:

"Pupil—You can really blow soap-bubbles with hydrogen?

Master—Yes, and here is a very big one; it separates from the soap-suds and rises like a balloon.

Pupil—Oh, how ripping!"

The difficulty for the reviewer is that we are dealing with the English translation and do not know the Ostwaldian equivalent of "ripping." The difficulty for the translator is that our boys do not speak the same slang as English boys and an American equivalent of this expletive is needed. Perhaps "Say, she's a peach!" would suffice, perhaps not, the problem is difficult. In all seriousness, is it necessary for a master of style, like Ostwald, to do this kind of thing to make a book "penetrating and lively?" E. R.

THE STUDY OF CHEMICAL COMPOSITION. An Account of Its Method and Historical Development, with Illustrative Quotations. By IDA FREUND, Staff Lecturer and Associate of Newnham College, Cambridge. Cambridge Physical Series. Cambridge: University Press. 1904. pp. 650. Price, 18 shillings, net.

The scope of this work may be best shown by giving the headings of the chapters:

Introduction; The Method of the Inductive Sciences. Chapter I., Theories of Combustion. II., Lavoisier and the Law of Conservation of Mass. III., Exact and Approximate Laws. IV., Berthelot and the Law of Mass Action. V., Proust and the Law of Fixed Ratios. VI., Dalton and the Law of Multiple Ratios. VII., Richter and the Law of Equiv-

alent Ratios. VIII., Combining or Equivalent Weights. Symbol Weights. IX., The Ultimate Constitution of Matter. Hypotheses prior to 1800. X., Dalton and the Atomic Hypothesis. XI., Gay-Lussac and the Law of the Combining Volumes of Gases. XII., Avogadro and the Molecular Hypothesis. XIII., Cannizzaro and the Application of Avogadro's Hypothesis to the Determination of Molecular and Atomic Weights. XIV., Petit and Dulong and the Law of Atomic Heat. XV., Mitscherlich and the Connection between Crystalline Form and Chemical Composition. XVI., Mendeléeff and the Periodic Law. XVII., Kekulé and the Law of Valency. XVIII., Berzelius and Isomerism. XIX., The Ultimate Constitution of Matter and the Genesis of the Elements.

The reader is surprised at the omission of the modern theory of solutions, of electrolytic dissociation, of freezing- and boiling-point methods of determining molecular weights and of the phase rule. Indeed, the names of Arrhenius and Willard Gibbs are not in the index. An extract from the preface will explain the author's position :

" * * * I was guided by the following considerations : the kind of historical treatment adhered to throughout the book seemed in this case unsuitable ; space was an object ; and as a matter of fact this subject is adequately dealt with in a number of text-books on physical chemistry, besides which a reprint renders the most important papers accessible."

While the omission is to be regretted in the interest of general readers, it is practically of no importance to the chemists and advanced students to whom this book is addressed. In this country, at least, the student is sure to give as much time to the fascinating study of physical chemistry as is its due and the space available for it in a book of this kind would permit only a brief statement of familiar things.

Miss Freund's method, as may be inferred from the headings, is to give, in each chapter, a detailed account of the work of a pioneer, followed by a careful study of the work of his successors in the particular field to the present time, thus presenting to the reader a charming series of monographs ; yet we find the chapters so connected by cross-references and historical continuity that the book is really "aus einem Guss" and in no sense a series of detached essays. The advantages of this method are obvious. For example, the reader desires to learn about the conservation of mass, he turns to the second chapter and finds the story of Lavoisier's investigations followed by that of Stas and of Morley's work on oxygen and hydrogen,

while the next chapter, on "Exact and Approximate Laws," gives a careful study of the results of the work of these three chemists, followed by Lord Rayleigh's work on nitrogen, the researches of Dulong and Arago and of Regnault on the compressibility of air and gases, the relation of the kinetic hypothesis to Boyle's law, Van der Waal's formula and, finally, Landolt's work on the conservation of mass.

In dealing with quantitative researches the author has not "merely stated the final results but has reproduced the values obtained in the actual measurements made, so as to indicate in each case the scope of the work involved and the degree of accuracy obtained."

Furthermore, the author has given "the actual words of those who have announced discoveries, who have described their own experimental investigations, or who have propounded new theoretical views." Thus Chapter IX. consists chiefly of quotations from Aristotle and Lucretius, from Bacon, Descartes, Boyle and Newton. The chapters on Dalton are full of quotations from his letters, his manuscript notes and his "System of Chemical Philosophy."

We have, indeed, a large and increasing number of reprints of important memoirs, but the hard-worked student, with examinations ahead, has little time to read them. If he is wise he will take the time to read and study Miss Freund's book, for nowhere can he find a presentation of the subjects discussed as clear, succinct and scholarly as this and some knowledge of these subjects is imperative.

Reference must be made to the chapter on Mitscherlich and his followers. In this country, the average course of the candidate for the Ph.D. degree, to-day, includes inorganic and organic chemistry, physical chemistry and physics. Few study mineralogy or crystallography. Many students and teachers are ignorant and remain ignorant of the connection between crystalline form and chemical composition. From this chapter of 74 admirably written pages, there is much instruction to be gained.

The last chapter closes with a review of the experimental evidence for the complexity of atoms and the identity of the ultimate constituents, including the work of Ramsey and J. J. Thomson and the work and speculations of Lockyer and Crookes.

Space considerations prevent a more detailed study of this book, but enough has been said to show its importance to all chemists. May it meet the reception it deserves. E. R.

ELEKTRIZITÄT UND MATERIE. Von J. J. THOMSON, Mitglied der Royal Society, Professor der Experimental physik an der Universität in Cambridge. Autorisierte Übersetzung von G. SIEBERT, mit 19 eingedruckten Abbildungen. Braunschweig: Druck und Verlag von Friedrich Vieweg und Sohn. 1904. pp. 100. Price, M. 3.

This is the authorized German translation of the well-known "Yale Lectures" by Prof. Thomson. The subject-matter is the work of this great leader in experimental physics. No one living has thrown as much light on the ultimate nature of matter as J. J. Thomson. We need only recall that, within the last 10 years, our conception of matter has undergone a fundamental change. In his celebrated paper "Die Überwindung des Wissenschaftlichen Materialismus," Ostwald pointed out that *matter is a pure hypothesis*. It was created in the imagination simply as a *carrier of energy*, which is all that we actually know to exist.

Thomson has since shown, by a series of brilliant experiments, that there is no occasion to assume the existence of matter. The *electron*, or unit electrical charge, under the conditions which exist in the atom, has all the properties that we are accustomed to ascribe to matter and there is, therefore, no occasion to assume the existence of what we ordinarily call matter.

These facts are discussed, especially in the fourth and fifth chapters of this book. The sixth and last chapter is devoted to the all-absorbing theme "Radioactivity and Radioactive Substances." These subjects are of as much interest and importance to the physical chemist as to the physicist. Indeed, no man of science, who would keep in touch with the newest and best in physics—the fundamental branch of natural science—can afford to remain unacquainted with this epoch-making work of J. J. Thomson.

The discussion of *valence* is of the greatest importance to the chemist. There is no subject in all chemistry which has been in a more unsatisfactory condition. The vagueness which has characterized the writings on valence for the last 20 years is due to the absence of any definite physical basis upon which to found this whole subject. Thomson points out that all valence is of an electrical nature, in a word, as was developed by the reviewer in his "Physical and Inorganic Chemistry," that the basis of chemical valence is Faraday's Law. With this exact conception as a starting-point, it is safe to predict that we shall hear less in the future of "free bonds" and that some real progress will be made in the consideration of chemical valence.

H. C. J.

ZUR BILDUNG DER OZEANISCHEN SALZABLAGERUNGEN. Von J. H. VAN'T HOFF. Erstes Heft, mit 34 eingedruckten Abbildungen. Braunschweig: Druck und Verlag von Friedrich Vieweg und Sohn. 1905. pp. 85. Price, M. 4.

The investigations of van 't Hoff to ascertain the conditions under which the great salt beds of the earth were deposited, are well known. The work has been carried on by van 't Hoff with the co-operation of Meyerhoffer and a number of students and assistants.

The contents of this first *Heft* has to do with crystallization, the effect of time, the effect of temperature, the effect of pressure and applications. This forms a completed chapter, as it were and, therefore, is published in this separate form. When this work, as a whole, is completed it will, undoubtedly, be another monumental contribution to science, to be added to the three which we already owe to van 't Hoff. H. C. J.

JAHRBUCH DER ELEKTROCHEMIE UND ANGEWANDTEN PHYSIKALISCHEN CHEMIE. Berichte über die Fortschritte des Jahres 1903. Herausgegeben von DR. HEINRICH DANNEEL, Privatdocent der physikalischen Chemie und der Elektrochemie der Technischen Hochschule zu Aachen. X Jahrgang. Halle, a. S.: Wilhelm Knapp. 1905. pp. 930. Price, M. 26.

It is only necessary to call attention to the appearance of the tenth annual issue of this valuable "Jahrbuch." This volume gives a complete review of all work that has a bearing on electrochemistry for the year 1903. The book is divided into a scientific and an applied part. The first comprises 529 pages, the latter the remainder of the work.

The reviews are, in general, satisfactorily prepared and the volume, as a whole, is very useful to any one engaged in research in electrochemistry, or who simply desires to follow what is being done by others. H. C. J.

PERCENTAGE TABLES FOR ELEMENTARY ANALYSIS. By LEO F. GUTTMANN, PH.D., A.C.G.I., A.I.C. London: Whittaker & Co.; New York: Macmillan & Co. 1904. Price, $1.00.

This small book of tables is designed to aid one in readily calculating the percentage of carbon and hydrogen in a substance which, upon combustion, yields carbon dioxide and water.

The percentages appear to be worked out with great accuracy as, in several cases, a difference of less than 0.01 and never greater than 0.02 was obtained between the calculated values and those given in these tables.

For any one having a number of combustions to make, the time saved by the use of this book would be a factor well worth taking into account. L. S. TAYLOR.